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ABSTRACT

Intended to assist Agency for International Development (AID) officers, advisors, and health officials in incorporating health planning into national plans for economic development, this first of ten manuals in the International Health Planning Methods Series deals with planning and evaluation of communicable disease control programs. The first four articles provide an overview of the subject and discuss specific aspects of the programs, such as program organization, surveillance systems, and immunization projects. Ten articles on specific diseases and disease types discuss malaria, tuberculosis, leprosy, veneral disease, filariasis, schistosomiasis, onchocerciasis, trachoma, bacterial enteric diseases, parasitic enteric diseases, and rabies. The papers outline the complexities of epidemiogologic interactions between disease-causing organisms, their reservoirs, and hosts in different geographic, climatologic, and cultural settings. (A supporting document in the International Health Reference Series containing a literature review and annotated bibliography is available separately as CE 024 223.) (YLB)

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International Health
Planning Methods Series

1

Communicable Diseases Control Planning

Guidelines for Analysis of Communicable Disease Control Planning in Developing Countries

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Guidelines for Analysis of Communicable Disease Control Planning

U.S. Department of Health, Education, and Welfare
Public Health Service
Office of the Assistant Secretary for Health
Office of International Health

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PREFACE TO THE SERIES

The International Health Planning Methods Series has been developed by the Office of International Health, Public Health Service on request of the Agency for International Development.

The series consists of ten basic volumes which cover a variety of health issues considered vital for effective development planning. These ten volumes are supplemented by six additional works in the International Health Reference Series, which list resource and reference material in the same subject areas.

The International Health Planning Methods Series is intended to assist health sector advisors, administrators and planners in countries where the Agency for International Development supports health related activities. Each manual attempts to be both a practical tool and a source book in a specialized area of concern. Contributors to these volumes are recognized authorities with many years of experience in specialized fields. Specific methods for collecting information and using it in the planning process are included in each manual.

The six supporting documents in the International Health Reference Series contain reports of literature surveys and bibliographies in selected subject areas. These are intended for the serious researcher and are less appropriate for broad field distribution.

The volumes in the International Health Planning Methods Series contain the collective effort of dozens of experienced professionals who have contributed knowledge, research and organizational skills. Through this effort they hope to provide the AID field officer and his host country counterparts with a systematic approach to health planning in developing countries.

PREFACE TO VOLUME ONE

This volume for the planning and evaluation of communicable disease control programs is the first volume in a series of works known collectively as the International Health Planning Methods Series.

The series was produced by the Office of International Health as requested by the Agency for International Development to provide AID officers, advisors and health officials in developing countries with critically needed guidelines for incorporating health planning into national plans for economic development.

Contributors to this volume include specialists and experts from various universities and national health research centers, who discuss specific aspects of disease control programs, such as program organization, surveillance systems, and immunization projects. Articles on specific disease and disease types include coverage of malaria, tuberculosis, leprosy, venereal disease, filariasis, schistosomiasis, onchocerciasis, trachoma, bacterial enteric diseases, parasitic enteric diseases and rabies.

The communicable diseases selected for inclusion in this manual constitute major public health problems in developing countries. Authors of the papers solicited for this manual were asked to present the current "state of the art" in the planning and evaluation of a specific disease control program.

The papers contained in this volume outline the complexities of epidemiologic interactions between disease causing organisms, their reservoirs and hosts in different geographic, climatologic and cultural settings. With an understanding of a disease and its epidemiologic correlates in a given setting, effective control methods can be planned and evaluated.

It is understood, of course, that no single manual or series of manuals can completely reduce the health care problems of developing countries to a rigid formula for success, because the epidemiology and available health care resources vary enormously from area to area. The authors of this manual, however, have provided a thorough understanding of the public health significance of each of the diseases discussed, and they have offered a systematic approach to planning and evaluation of disease control programs.

Preparation of this volume was undertaken for the Office of International Health by the E.H. White & Co., Management Consultants, of San Francisco, California. Articles in this volume were compiled by James Chin and Florence R. Morrison. James Chin, M.D., M.P.H., is chief of the Infectious Disease Section, California Department of Health Services at Berkeley. He is also lecturer in Epidemiology at the School of Public Health, University of California. Florence R. Morrison, M.A., is head of the Statistical Services Unit, Infectious Disease Section, California Department of Health Services.

Chin and Morrison also contributed the first article in this volume, "Communicable Disease Control", which provides an overview of the subject and some important background to introduce the more specialized articles to follow.

An effort has been made to blend detailed expert knowledge with practical advise and insight. While it remains dependent upon variable local conditions, this manual does provide firm guidelines for each of the interest areas discussed.

Contributors to this manual, in addition to describing the technical aspects of a particular communicable disease control program, have also expressed their personal viewpoints on the current status of these programs in developing countries. While their viewpoints generally coincide with those of the organizations or agencies with whom they are associated, the material in this manual should not be construed to reflect the official policy of any agency or organization.

The control of communicable disease is a critical health problem in developing countries. This volume, it is hoped, will assist in effectively evaluating current programs, and it should provide a sound basis for planning various types of communicable disease control programs within the context of national development planning.

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ACKNOWLEDGMENTS

Each volume in the International Health Planning Methods Series has been the work of many people. In addition to the primary authors, each manual has involved government reviewers and reviewers from positions outside government, editors, revisors, and numerous technical and support personnel. Substantial contributions have been made by manual advisors who provided the authors with the benefit of their knowledge and experience in the fields of study.

With reference to Volume 1: Communicable Disease Control Planning, special thanks are in order for contributions made by advisor Dr. Phil Brachman.

Dr. Robert DeCaires and Lynn Beamer have provided valuable advice for several volumes in the series.

Contributors to this volume include: Karl A. Western, Stanley I. Music, A. N. Angle, S.O. Foster, R.C. Hogan, J.S. Weisfeld, Robert M. Worth, Laurence S. Farer, Merlin L. Brubaker, Roger A. Feldman, Frederick L. Dunn, Chandler R. Dawson, Julius Schachter, George W. Beran, Robert S. Desowitz, William Chin, Richard C. Collins, and Donald Heyneman.

While the present work could not have been completed without the assistance of many contributors, responsibility for the content of this manual rests solely with the authors.

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COMMUNICABLE DISEASE CONTROL

by

James Chin and Florence R. Morrison

Infectious diseases, for the purpose of this manual considered to be synonymous with communicable diseases, have been studied extensively during the past century. These studies have led in most developed countries to effective control of the major life threatening infectious diseases. However, the geographic concentration of some infectious diseases, compounded by lack of resources and commitment to prevent them, are reflected in their continued presence as significant public health problems in developing countries.

Infectious diseases are caused by many hundreds of known agents. Even if grouped, the list of discrete agents and the diseases they cause would number several hundred. Despite the multitude of disease causing organisms, only a dozen or so illnesses or groups of illnesses include almost all the maladies for which any significant control can be expected in developing countries. Each of these illnesses or groups of illnesses can be considered a specialty unto itself. The medical literature which describes these organisms contains hundreds of citations for many, and thousands for some. Therefore, it required an individual with experience in the developing countries to write about the planning and evaluation of a control program for each. Such authors were enlisted in the preparation of this manual.

This manual should not be used as a rigid blueprint for the planning and evaluation of all communicable disease programs in any developing country, because the epidemiology and the existing medical care systems and resources vary so much from area to area. However, this manual should be useful to health assessment teams, health administrators, health workers, and public health students by giving them: (1) an understanding of the epidemiology and public health significance of the infectious diseases discussed and (2) a general approach to planning and evaluation of control programs.

Infectious Diseases of Importance in Developing Countries

Recently, all the member states of WHO in Asia and Africa, south of the Sahara, were asked to list what they considered to be their most important public health problems. The consolidated list was as follows (roughly in their perceived order of importance):

Malaria and other parasitic diseases
Tuberculosis
Malnutrition

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Diarrheal diseases
Leprosy
Respiratory diseases (other than tuberculosis)
Venereal diseases
Measles
Poliomyelitis
Tetanus (mainly neonatal)

With the exception of malnutrition, all of the diseases listed are infectious. Of those infectious diseases perceived by these member states to have the greatest public health significance, only respiratory diseases (other than tuberculosis) and diarrheal diseases have no well-defined control or preventive measures. All of the diseases listed are included in this manual except for respiratory diseases (other than tuberculosis), for which control has not been achieved even in developed countries. In addition, the following infectious diseases which also constitute significant problems in developing countries and which have relatively well-defined control and/or preventive measures have been included: filariasis, schistosomiasis, onchocerciasis, trachoma, and rabies.

The Epidemiology of Infectious Diseases

Planning and evaluation of infectious disease control programs are dependent upon a thorough understanding of the epidemiology of these diseases. It is beyond the scope of this manual to provide a detailed description of infectious disease epidemiology. However, a brief presentation of the definition and significance of basic variables which contribute to an understanding of infectious disease would be helpful.

Epidemiology can be defined as the study of the factors which influence or determine the distribution of disease in population groups. Epidemiology is a relatively recent medical science which did not exist as a formal discipline until the mid-19th century. The acknowledged father of epidemiology, Dr. John Snow, observed in 1854 that cases of cholera in London were associated with one particular water supply. By associating cases of cholera with their water supplies, he was able to conclude that water supplied by one company via the Broad Street pump was the major source of the cholera epidemic. Dr. Snow used what are now considered basic epidemiologic methods. These include critical evaluation of collected data and the utilization of comparisons, i.e., the use of statistical methods and control groups. In simple terms, the epidemiologist tries to determine who and of whom has developed what, when, where, and why. The "who" represents cases and the "of whom" is the population from which the cases are occurring. The accurate ascertainment of both numbers is of paramount importance in epidemiologic investigations in order to calculate rates ("who" = numerator and "of whom" = denominator) to compare disease experience in different populations.

Infectious diseases are the result of interaction between several independent but essential factors. These include the:

causative (etiologic) agent,
host,
environment,
reservoir, and
modes of transmission of infection.

Following is a brief description of each of these factors. Infectious disease agents are parasitic organisms which range in size from viruses which can be visualized only by an electron microscope to tapeworms which may be many feet in length. In the great majority of cases, these parasitic agents do no noticeable harm to their hosts, except when present in overwhelming numbers. In several instances, notably the elaboration of specific toxins and destruction of host tissue, their growth can cause severe adverse effects and even threaten the host's existence.

Many attributes of the causative (etiologic) agent are important in the initiation of infection and disease. They include:

Type of Agent: Infectious diseases are caused by microorganisms which are summarized in Table 1 on page 4. Knowledge of the etiologic agent for a disease suggests its mission; reservoir of infection; intermediate hosts, if any; area of occurrence; specific treatment; and control methods.

Virulence/Pathogenicity: The ability of an infectious agent to induce disease and its relative invasiveness are measured by the extent of tissue damage in the host. For example, plague bacillus is highly virulent for man; whereas, the common cold virus is usually of low virulence. Both organisms are pathogenic in that they have the ability of produce disease in man.

Resistance of the Agent to Environmental Factors: The relative resistance of a particular agent to environmental factors dictates how the agent is best transmitted. The etiologic agents of sexually transmitted diseases cannot survive well outside of the human host; whereas, those agents which are transmitted via soil, such as the bacteria which cause tetanus or botulism, can withstand severe environmental conditions.

Infectivity or the Infecting Dose: This refers to the number of organisms needed to initiate an infection. For some agents, such as poliomyelitis, only a few viruses are needed; for others, such as cholera, up to 100 million organisms may be required.

Many host factors are of great importance in determining the frequency and severity of infectious diseases. Biological host factors include age, sex, race, genetic constitution, and presence of other diseases. Other host factors include social class, economic class, nutritional factors, cultural factors, marital status, lifestyle, personal hygiene. These factors influence or determine the exposure of persons to various infectious disease agents and, after infection, the ability of the individual to deal with his disease.

To a marked degree, environmental factors affect the transmission of infectious disease agents, host susceptibility to infection, and subsequent development of disease. These factors include climate (temperature, humidity, sunlight, season, prevailing winds, rainfall), residence, occupation, environmental sanitation, spatial and geographic location.

The term reservoir of infection refers to the natural habitat of the infectious disease agent, i.e., where it usually lives and multiplies. Most agents have known primary reservoirs. Familiarity with these reservoirs (or sources of infection) is needed to direct control efforts.

Human--For many infectious disease agents, such as smallpox, measles, syphilis, typhoid, cholera, etc., man is the

Table 1

INFECTIOUS DISEASE AGENTS

Agent	Description	Examples/Disease
Virus	Submicroscopic size; one of the simplest forms of living matter; cannot survive or replicate outside of a living cell; not susceptible to antibiotics or drugs.	Measles, Poliomyelitis, Smallpox, Rabies
Bacteria	Submicroscopic size; most can be grown in a variety of artificial media; most are susceptible to a variety of antibiotics	Diphtheria, Leprosy, Tuberculosis, Typhoid, Cholera, Shigellosis
Rickettsia	Specialized small bacteria, microscopic size which are obligate intracellular parasites; susceptible to certain antibiotics; must be grown in laboratory animals, embryonated eggs, or cell culture systems.	Typhus, Q-fever, Rocky Mountain spotted fever
Chlamydia	Microscopic size; can be regarded as bacteria which are restricted to intracellular existence: susceptible to the broad spectrum antibiotics.	Trachoma, Lymphogranuloma venereum, Psittacosis
Protozoa	Microscopic size; single cell parasites; with varied life forms, cycles; susceptible to some drugs.	Malaria, Trypanosomiasis, Amebiasis
Metazoa	Relatively large multicellular parasitic "worms" with complex life cycles and intermediate hosts; treatment usually restricted to relatively toxic drugs.	Filariasis, Onchocerciasis, Schistosomiasis
Fungus	A complex grouping of unicellular and colonial organisms including mushrooms, molds, yeasts, and types which can be both free-living and parasitic in human or animan tissues; microscopic to large size; susceptible only to special drugs.	Athlete's foot, Ringworm, Histoplasmosis, Thrush

principal reservoir.

Animals--For diseases, such as rabies, salmonella, Q-fever, and psittacosis, animals constitute the primary reservoir or source of infection.

Environment--The agents for diseases such as tetanus, botulism, coccidioidomycosis, and others, are normally found in soil.

The control of infectious diseases is dependent upon knowledge of the mode(s) of transmission of the causative agent. The following table summarizes the important modes of transmission:

Mode of Transmission	Disease Examples
Person-to-person contact	Sexually transmitted diseases--syphilis, gonorrhea, etc.--and leprosy(?)
Ingestion	Salmonella, typhoid, shigella, amebiasis
Airborne	Tuberculosis, Q-fever, occidiomycosis
Vector borne	Malaria, filariasis, rabies onchocerciasis
Percutaneous	Schistosomiasis, hookworm, tetanus
Congenital	Rubella, Toxoplasmosis, syphilis

Other common terms used in infectious disease epidemiology include the following:[2]

Endemic: The constant presence of a disease or infectious agent within a given geographic area; may also refer to the usual prevalence of a given disease within such area. Hyperendemic expresses a persistent intense transmission, e.g. malaria.

Epidemic: The occurrence in a community or region of cases of an illness (or an outbreak) clearly in excess of normal expectancy and derived from a common or a propagated source.

Inapparent or Subclinical Infection: The presence of infection in a host without occurrence of recognizable clinical signs or symptoms. Inapparent infections are identifiable only by laboratory means.

Incidence: The number of new cases of a specified disease diagnosed or reported in a given period. One year is the usual time period though other periods--one month, six months, several years--may be used.

Prevalence: The number of cases of a specified disease or the number of persons with a particular symptom or condition which exist at a given time in a given population, regardless of when the illness, symptom, or condition may have begun.

Control and Preventive Methods

Immunization is the first method to be discussed here. The ancient Chinese observed that if an individual was deliberately innoculated with material from the skin lesions of a case of smallpox, the resulting infection was much less severe and the individual would, thereafter, be protected against smallpox. This process, called variolation (although less dangerous than natural acquisition of smallpox was, nevertheless, relatively hazardous) represented man's first effort to immunize or protect humans against infectious disease.

The first human vaccine was developed by Jenner in 1798. He had noted that human infections with cowpox (a disease of cattle similar to smallpox in man) protected a person from subsequent attack of smallpox. Jenner used cowpox (vaccinia) lesions to immunize persons against subsequent infection with smallpox.

Modern vaccines consist of either killed (inactivated) or live attenuated (modified or weakened) infectious disease agents and are used to immunize persons against disease due to these agents. Smallpox vaccine (vaccinia) and vaccines which have been developed during the past 50 years constitute the most successful measure available to prevent infectious diseases. Of all the control/preventive measures, vaccines are by far the most effective and least expensive. Unfortunately, effective vaccines are not available for all infectious diseases.

Case finding and treatment are also control methods. Effective drugs and antibiotics for treatment of many severe nonviral infectious diseases have been available only during the past 30 to 40 years. Rapid identification and treatment of cases and close contacts constitute a very important method of control and/or prevention, especially for those diseases against which no effective vaccine is available. Effective treatment, aside from minimizing morbidity and mortality in an affected individual, also rapidly renders that individual noninfectious and, thereby, reduces the spread of disease to others.

Control of insect or animal vectors and intermediate hosts is very important. For diseases transmitted via an intermediate host or an insect or animal vector, control and/or prevention can be accomplished by reducing or eliminating human exposure to these fectors. Human rabies can be prevented by avoiding exposure to potentially rabid animals and by immunization of domestic animals which may develop rabies. Malaria could be prevented, for example, by eliminating the mosquito vector and schistosomiasis could be effectively prevented if the snail intermediate host(s) were eradicated. Control or elimination of these insect or animal species is difficult and expensive but can be accomplished in localized areas if sufficient resources are expended.

Improved environmental sanitation is a key factor. For disease spread primarily by the fecal-oral route, effective control and prevention can be achieved by improved environmental sanitation. It has been amply demonstrated that sewage disposal systems and pure water supplies result in a marked decrease in enteric diseases.

Health education is critical. Awareness of how infectious diseases are spread can result in personal and community efforts to avoid exposure to infections. However, knowledge is not enough. People must also be motivated to act on the information received. For example, health education about how venereal diseases are acquired results only in knowledgeable individuals with venereal disease unless awareness of the problem motivates individuals to accept available preventive methods.

Data Considerations

Each paper in this manual and the literature review discusses the data required to plan and evaluate specific communicable disease control programs. Different diseases may require various kinds of information at different stages in a control program. For example, egg counts for schistosomiasis and other helminthoses might be wanted only after a control program had been in existence for sometime; sero-conversion rates for children immunized against measles would be required early in control efforts; individuals found to have sputum smears positive for tuberculosis would be information needed to plan control efforts.

It is not necessary to have exhaustive data for a given disease in order to consider a control program. But clearly, some data must be available before any planning can be done to control a disease. It must first be determined that disease A is a problem, then the answers to the following questions are needed:

Is disease A a more serious problem than disease B?

What proportion of illnesses or deaths does it cause compared with other diseases that affect the population?

What population groups (age, sex, area, etc.) are most severely affected:

Does it attack the productive portion of the population?

Does it create a great burden for those who are well because it completely incapacitates its victims but does not cause death?

Does it have other deleterious effects?

Are effective control or preventive methods available for this disease; and if so, how expensive are they?

The answers to questions like those above will help planners to make a decision about initiating a control program.

Once a decision is made to initiate a control program, or to study the feasibility of controlling a given communicable disease, the paucity of data or its poor quality should not be a deterrent. One of the goals of the program might very well be to collect additional data and then to correct and refine it. The newer, more accurate data can then be used to redirect and evaluate the first efforts at control. This process can be repeated until the program has the data needed for program planning and evaluation at a more definitive and sophisticated level.

Data on disease occurrence and severity can be obtained from a variety of sources, none of which may be complete, but which when merged, may give an idea about the extant and burden on the population of a particular disease. Death records are probably most frequently available in developing countries, especially in urban areas. Death data will indicate which diseases or conditions account for the greatest proportion of all deaths, whether males or females are affected most, as well as which age groups, in what region of the country, at what season of the year, and perhaps other factors. Of course, those diseases which may be widespread but not ordinarily fatal will not be represented. Other shortcomings of death data may be better registration of death in urban areas; poor registration of early infant deaths and misclassification in cause of death. Hospital (inpatient) and clinic (outpatient) records may also be useful as an indication of what illnesses are most frequently seen for treatment. Again these records probably underrepresent disease in rural areas where medical and clinic facilities are scarce; they usually represent the most serious illnesses in a community; they are subject to misdiagnosis as well as other inaccuracies and biases found in most such records. Other sources of data may be practicing physicians, paramedics, midwives, schools, businesses which have a large labor force, village elders or headmen, pharmacists, police, and religious leaders.

Basic methods of collecting communicable disease data are simple surveys or surveillance systems. Either method may be used exclusively or both may be combined for greater effectiveness.

Sampling or Surveys: With modern statistical and sampling methods, data on a given disease and the population in which it arises can readily be obtained. Sampling has many advantages over registration or surveillance systems: speed, adaptibility, greater accuracy, and lower-cost data. Sampling is not an efficient or inexpensive method if used to obtain information about rare diseases or conditions. However, the diseases discussed in this manual are all widely distributed in most developing countries. Another advantage of sampling or surveys is that they can be designed to obtain answers to questions which may arise suddenly in contrast to the restricted set of items available on surveillance forms printed long ago. In those countries where no permanent statistical systems exist, sampling may well be the only rapid method to obtain necessary data. Sample surveys can also be utilized to delineate the characteristics of the general population when no census information is available. Because surveys are time-limited rather than permanent, ongoing systems, it may be easier to employ sampling experts to assist in designing, executing and preparing sample estimates than it is to hire such professionals on a long-term basis. WHO has had a good deal of experience in sampling for infectious diseases and can probably provide most of the expertise required.

Surveillance Systems: In contrast to sample surveys, these are usually designed for long-term use. Such systems provide data on trends of various infectious diseases over time so that the natural history of the disease and its epidemiology can be studied. This sort of information is usually not available through surveys. Surveillance data may also explicate regional, climatic, and occupational differences in disease occurrence over long periods of time. However, surveillance systems are most costly, give less accurate data are subject to variations in underreporting by physicians, by area, by various host factors, and perhaps many other factors. In addition, it is very difficult to estimate biases in surveillance data if such a system is relied on exclusively. However, such systems are simpler and may not require statistical or sampling experts or other trained professionals.

Combination of Methods: In many developing countries, a combination of both systems may be most utilitarian. Surveys could be used to determine accurately disease prevalence and the characteristics of the people affected. This information could then be used for planning a control program. During the control phase of the program, surveillance could be developed to monitor disease trends, gather additional information about the epidemiology of the disease and delineate the characteristics of the population newly affected. For evaluation purposes, a resurvey can be made to determine with precision how control efforts affected disease prevalence. Such a combination of techniques is most effective since it allows control personnel to take various other factors into account in making program assessments. Furthermore, a comparison of the data obtained by the two methods may point out specific problems and biases in one or the other method. If surveillance alone is used, greater reliance must be placed on death, hospital, and clinic records; and the less severe end of the disease spectrum will generally go undetected. (See also papers on Surveillance and Immunization Programs for additional discussion on sources and systems for collecting infectious disease data.)

Practical Considerations

Determination of priorities must take place. The objective and orderly assignment of disease control priorities is theoretically simple. Consideration of factors, such as incidence, prevalence, disease severity, and availability of effective and inexpensive control methods, will enable some ranking of disease control priorities. Smallpox in the developing countries during the 1960s merited the highest priority because of its great incidence and severity; and because a relatively simple, highly effective control method--ring vaccination around cases--was availabe. The successful WHO smallpox eradication program attests to the wisdom of assigning this program top priority. However, after smallpox eradication--what next? There is no other infectious disease which can be given as high a priority as smallpox had.

Control versus eradication remains an issue. At the present time, with the possible exception of yaws, we cannot realistically consider global eradication of any other infectious disease. However, eradication of some diseases from defined areas should be attempted when epidemiologic conditions permit--e.g., geographically limited areas, especially islands can be rendered free of malaria, rabies, etc.--but the logistics and expense of disease eradication over extensive land masses makes this goal unattainable in most current situations. In recognition of this situation, WHO has embarked on programs, including an expanded immunization program to control several major infectious diseases in developing countries.

During the past two decades, there has been an increasing acceptance of the principle that specific infectious disease control programs should be merged into integrated disease control programs whenever possible. This view has been espoused as policy by WHO and is echoed in most of the disease control papers contained in this manual. Aside from considerations, such as whether an infectious disease control program should be vertical (separate) or horizontal (integrated), the administrative organization of epidemiology, laboratory, and statistical services deserves some comment. An effective disease control program is dependent upon good, functional working relationships among these services. Too often, these services are administratively and physically separated. Separation can lead to conflicts about program priorities, allocation of resources, and the kind of services which should be provided. Such problems may develop regardless of the organizational structure if good personal working relationships are not present. Any existant administrative barriers between these services should be removed and at a minimum, effective communication developed and promoted.

Competition for health resources persists. Unfortunately, infectious disease control programs have to compete for health funds which are exceedingly scarce in most developing countries. It is generally acknowledged that control and/or prevention of infectious diseases is both more logical and more cost effective than the continued treatment of infected persons, many of whom are rapidly reinfected. In contrast to the rapid and often dramatic effects of treatment, the benefits from control and prevention are not usually apparent for many years. Thus, the pressures to continue to use limited resources to support and augment the existing medical care system are great. As a result, the planning and implementation of preventive programs may, in many instances, require outside commitment and support. Decisions about allocation of available resources in developing countries are emphatically more difficult when other major problems, e.g., nutrition and family planning, are considered.

Some authorities have maintained that since many, if not most, of the major problems of developing countries will, even without any specific control programs, improve concomitant with economic development, scarce resources need not be diverted to such control programs. This view, however, neglects some very important economic reasons to undertake disease control measures. As noted in the papers in this manual on onchocerciasis, schistosomiasis, and filariasis, widespread infectious diseases can be associated with loss to cultivation of the most fertile lands in less economically advanced regions. The presence of such diseases perpetuates an outmoded agrarian economy which, in turn, makes economic progress unlikely. Furthermore, illness due to infectious disease weakens the labor force, reduces productivity, and burdens the community with the costs of treating or supporting those incapacitated by illness. Thus, there are cogent economic reasons to reduce the level of infectious diseases in developing countries without waiting for the uncertain, slow pace of economic development. Specific and effective control methods which are available should be used to alleviate the unacceptable toll of infectious disease currently present in most developing countries.

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ORGANIZATION AND ADMINISTRATION

by

Karl A. Western

While communicable diseases no longer are the leading causes of morbidity and mortality in Europe and North America, the general consensus is that their rank has changed very little this past generation in most of the developing world. The word "consensus" is used deliberately because the absence of accurate information about the actual levels and adverse health effects of communicable diseases in developing countries is nearly universal. The World Health Statistics Annual (1972), for example, provides mortality data for only one country in Africa (Mauritius) and four in Asia (Hong Kong, Israel, Japan, and Thailand).[1]

Since one unofficial indicator of development among nations is the ability to generate meaningful statistics and biomedical data, it is inevitable that communicable disease specialists and policy makers must continue to make policy and program decisions which are based on guesses rather than estimates based on hard data. This is disturbing primarily because it is technically feasible to do a better job of gathering epidemiologic information on communicable diseases in developing countries. Public health administrators concerned with prevention rarely have the information they require at hand before they are forced to make decisions.

A more serious concern is the view expressed by technicians that communicable disease prevention and control in many areas of the tropics have deteriorated in recent years and the implication that conditions will continue to get worse.[2] This opinion is usually expressed privately rather than in print and, as should be obvious from the preceding paragraphs, is impossible to substantiate except in striking circumstances such as the collapse of the malaria eradication program in Sri Lanka. The reasons put forward are complex and no single factor is responsible.[3,4] Prominent factors are:

(1) the deterioration of disease control programs in the post-colonial period (since 1950);
(2) increasing population;
(3) population congestion, particularly in urban areas;
(4) inadequate environmental sanitation;
(5) lack of well-trained nationals to supervise programs;
(6) technical obstacles such as insecticide-resistance of mosquitoes which transmit malaria and dengue fever;
(7) lack of appropriate technology to prevent or control important tropical diseases;

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(8) preventive programs losing the struggle with clinical services for limited health funds.

The checkered progress of communicable disease control in the developing world makes it imperative to review the organization and administration of these programs in a constructive fashion. This paper will first deal briefly with the origins of communicable disease control in Europe and North America in order to put the situation in tropical countries into historical perspective. Then, the traditional organization of communicable disease programs in the colonial period (approximately 1870-1950) will be summarized. The third section will present the current general health policies and strategies of developing countries, primarily through the recommendation of the World Health Assembly. This section is necessary background to the fourth section in which the current organization and administration of communicable disease services are outlined. The final section presents strategies for improving the effectiveness of communicable disease prevention and control in the developing world.

The following assessment of the organization and administration of communicable disease control in developing countries is based on the author's experience as a Regional Officer with the Pan American Health Organization (PAHO) over the last several years. This experience is somewhere between that of a national administrator whose responsibility is confined to one country and other international workers who have the impossible task of maintaining familiarity with programs on a global basis. The Region of the Americas can claim to be the most diverse. Economically, the gamut runs from extremely poor countries to the most wealthy. The majority of countries are now classified as in the intermediate or advanced stages of development. Each Latin American country, as is shown in the next section, has evolved its own health system. The Region accommodates member governments with diverse political philosophies. While the United States of America is the major donor country, the membership of France, the Netherlands, and the United Kingdom in PAHO and their influence on the associated territories in the Caribbean provide experience with communicable disease control programs in these systems also. Finally, the majority of references in the communicable disease literature focus on Africa or Asia. This effort, which emphasizes Latin America and the Caribbean, may flesh out the picture.

Origins of Communicable Disease Control Activities

Primitive quarantine methods which originated in antiquity were based on empirical observations of the spread of dread diseases from infected visitors to other members of the community. Organized communicable disease control activities became possible in the early nineteenth century with the development of accurate mortality figures and disease reporting in England under the inspired Leadership of William Farr. Early epidemiologists, such as John Snow who studied cholera, were able to utilize these data to calculate attack rates for defined groups, compare attack rates between populations, and postulate the probable mode of transmission of disease. Snow's analysis implicated water-borne disease that originated from a single company.[5] His findings also led to the first control measures based on scientific observations and tests of hypotheses. It should be pointed out that Snow published his work in 1855, just two years before Pasteur announced his conclusion that fermentation was due to microorganisms, thus launching microbacteriology and the "germ" theory of disease.

These momentous events occurred in the midst of the Industrial Revolution which produced the migration of rural populations into rapidly swelling cities and new towns. No administrative or legislative framework existed to deal with sewage and garbage disposal or provide safe drinking water and food. The response in England and the United States was to place responsibility for infection control squarely with the local authorities. Local boards of health and medical health officers were established by local initiative and charged with the responsibility to control infectious diseases. In the absence of effective medications, vaccines (except for smallpox), and pesticides, their efforts necessarily focused on environmental measures, surveillance of notifiable diseases, and quarantine.[6,7]

The Industrial Revolution came somewhat later to France and the organization of public health services was made difficult by the political turmoil of the Revolution, the Napoleonic regime, and Restoration, and the Third Republic. Central authority was stronger in France and, as a result, local public health councils were created by national law as early as 1848. Throughout the various regimes, however, the councils depended on the local prefect and had advisory functions only. Germany faced similar problems with a significant difference--there was no united Germany. The question of health organization was intimately linked with the objectives of national unification. German leaders first formulated the concept that society has an obligation to protect and insure the health of its members and eventually created the first national public health organization in 1876. The Germans were also pioneers in recognizing the essential role of the laboratory in environmental sanitation and communicable disease control.[8]

This brief summary of the historical origins of communicable disease control programs was included for two reasons. The first is that socioeconomic conditions in the developing countries are in many ways reminiscent of the phenomena observed in Europe and North America during the first Industrial Revolution. Indeed, many of the countries are looking towards industrialization as the means to achieve socioeconomic development. The second reason is that the European colonial powers have had a profound influence on the development of the preventive medical services throughout Asia and Africa. After achievement of independence, this influence continues to be felt through the infrastructure left behind, the training given to national technicians and administrators, and the bilateral assistance in disease prevention and control provided to developing countries. Latin America achieved independence from Spain or Portugal before the formation of public health services in those countries. As a result, independent institutions have developed in each country in communicable disease control. The Latin American systems, nonetheless, incorporate to varying degrees the elements of the English, French, and German systems. While central planning and authority predominate rather than local control, and commitment to laboratory support and the provision of service through insurance and "seguro social" schemes are striking in contrast to other regions.

Despite technical advance in vaccine development, antibiotics, and vector control, developing countries are confronted with the same problems which faced their European counterparts 150 years ago. With improved communications, simplified surveillance systems, computer-based data processing, more rapid laboratory diagnostic procedures, preventive measures to supplement improved environmental sanitation, and applied research for diseases in which effective public health measures do not exist, there are grounds for optimism that many developing countries can reduce the toll of communicable diseases and achieve the ambitious objectives adopted by the World Health Assembly.[9]

Traditional Organization in Developing Countries

During the period between the organization of communicable disease programs in Europe and North America and the end of the colonial era (approximately 1870-1950), communicable disease control in the tropics was patterned and often administered by technicians from developed countries, but with different objectives. First priority was usually given to the endemic tropical diseases which were likely to kill or cripple the expatriate staff, the economically productive work force, or livestock. Programs directed towards communicable disease prevalent in the indigenous women or children were given considerably lower priority. Even programs which included women and children, such as the Rockefeller Hookworm Control Programs in Latin America and the Caribbean, basically did so for economic reasons. The option of improving environmental sanitation so successful in Europe and North America was not adopted on a large scale because of three main reasons. First, the majority of the population in the tropics remained rural and dispersed, which created incredible logistical problems. Second, the price would have been prohibitive. And third, medical advances created other approaches with a more immediate impact on death and illness at what appeared to be a lower cost.

The approach to communicable disease control planning was simple and direct. If a canal or railroad project could not be completed because the workmen were falling ill or could not be recruited because of malaria, yellow fever, or cholera, these were the priority diseases. Commissions to study the problem locally and develop strategies for prevention and control were the order of the day. These commissions naturally attracted administrators and scientists who arrived with or soon developed strong interest in individual diseases. The final result was the development of a small number of disease prevention and control programs each directed towards a single disease. Each program had a separate administrator, budget, field staff, transport, communications, and surveillance system. Operational norms and guidelines were developed at the program level. In some programs, most notably the malaria campaigns, the field operations had a paramilitary flavor with uniforms, rank, and strict discipline. It was usual for these categorical ("vertical") disease control programs to be located within the ministry or agency responsible for health, but free-standing commissions or institutes were common. Even if the malaria, yellow fever (Aedes aegypti), tuberculosis, smallpox, and leprosy programs were in the same agency, coordinated services seldom existed or, for that matter, were considered desirable.

The termination of the colonial period coincided with the explosion of medical technology during and after World War II. Particularly pertinent for this discussion were the development of DDT, the discovery and mass production of penicillin and antimalarials, and the availability of improved yellow fever and smallpox vaccines. Within the space of several years, the concept of disease control was replaced by eradication of malaria, Aedes aegypti (the jungle mosquito vectors of yellow fever would not be affected by household insecticide spraying), yaws, and smallpox. The attraction of eradication programs to specialists, administrators, economists, politicians, and funding agencies was obvious. An intensive, sustained effort against the targeted disease with adequate funding would rid the population of a traditional scourge forever. To be effective, neighboring countries or preferably whole continents should embark on the eradication effort in coordination. Allocation of a disproportionate amount of the health budget to the attack and consolidation phase could be justified by the lower costs of maintenance once eradication had been achieved and the eventual savings garnered by not having to fund a disease control effort year after year. The theory was that the funds available following eradication would be plowed back into the next disease scheduled for eradication or general health services. The eradication staff and infrastructure would also be retrained and either utilized in subsequent eradication efforts or integrated into other control programs.

Eradication efforts met with varying degrees of success: the most striking has been the recent global eradication of human-to-human smallpox transmission.[10] Yaws has now been eliminated from most developing countries and, where it persists, is confined to remote areas where populations are dispersed. Urban yellow fever no longer occurs, though the threat persists. A major portion of South America is now free of Aedes aegypti and both yellow fever and dengue. Europe, the Middle East, the Caribbean, the temperate areas of South America, and many of the Western Pacific islands have virtually eliminated endemic malaria transmission.

Despite the initial enthusiasm and the considerable progress achieved through eradication programs, the concept has gradually lost credibility and may be abandoned. The major technical reasons might be summarized as follows:

(1) lack of appreciation of the complex epidemiology of diseases;
(2) misplaced faith in the "hard immunity" concept;
(3) overestimation of the decrease in disease levels through intervention with a single control measure;
(4) inability to carry the eradication effort to that final patient or vector;
(5) failure to anticipate the massive effort required in maintaining areas free of the disease prior to final eradication;
(6) difficulty in sustaining the eradication effort when the targeted disease disappeared from the population and administrators perceived the program as being less cost-effective;
(7) the emergence of technical problems, such as insecticide and drug resistance.

The technical problems of eradication have been emphasized because considerable publicity has been given to the political problems and interruption of funding which plagued some unsuccessful programs. Even if these factors had been minimized, total eradication on a global basis still would not have been attained. Currently, there is less support among technicians for eradication efforts than among the policy makers. The PAHO Advisory Committee on Dengue, Yellow Fever, and Aedes aegypti, for example, recommended a more flexible policy towards eradication of Aedes aegypti only to have the policy making Directing Council reaffirm the 1947 Regional Eradication Strategy.[11] Now that smallpox has been eradicated, further proof of the eradication concept's disrepute is that no other WHO-supported communicable disease control program has eradication as its final objective. It has been proposed that yaws eradication be considered but that the initial effort be directed at the Americas.[12] New WHO programs, such as the Expanded Program on Immunization and the Prevention of Blindness, clearly are directed at control.

Current Health Policies in Developing Countries

Disenchantment with single disease control programs and efforts at eradication coincided with rising expectations with regard to health in developing countries. This attitude is reflected in the constitution of the World Health Organization which includes the often quoted definition of health as "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity."[13] Subsequent operational definitions of this ideal continue this holistic approach to health.[14]

The standards for health care policies in developing countries are best sought in the resolutions adopted each year by the World Health Assembly. Basic health services are to be provided to the greatest number of people as soon as possible. Maximal use should be made of the health care infrastructure in the provision of these basic services. The infrastructure should also be extended as rapidly as possible to areas which presently receive no organized medical services. Developing countries implicitly accept the implication that rapid extension of coverage may not be possible without sacrifices in the quality of care. It is also recognized that developing countries will not be able to afford the luxury of separate programs for each of the important communicable diseases.

The formulation of these far-reaching health policies occurred in a setting in which the international lending and technical assistance agencies operated on the assumption that improved health could best be achieved through general socioeconomic development rather than health programs. A large segment of the international community was also convinced that the population explosion was the greatest problem facing the developing world and that the top priority should be to reduce birth rates, not death and disease. Indeed, communicable disease control programs were held at least partially culpable for the predicament of saving lives without concern for the demographic consequences.

An accommodation of sorts has been reached among these different policy approaches. It is now appreciated that total reliance on economic development will take several generations before spin-offs in health become apparent and will not meet the demands of an increasingly articulate Third World population for health services.

The need for population control is also accepted, but experience has shown that children function as a form of insurance in developing countries and parents will not voluntarily reduce their family size without some assurance that their first children will survive to adulthood. Family planning, therefore, is increasingly promoted within the context of maternal-child health and primary health services.

It is also expected that communicable disease control programs will also be incorporated into the primary health care programs in so far as it is possible. The current dilemma of communicable disease program managers and specialists is that this policy has been formulated and adopted at the theoretical level. In actual fact, there are very few examples anywhere of effective communicable disease control in an integrated program. The examples which do come to mind (China, Cuba) relied very heavily on a vertical approach in the early phases. With Cuba, the case can also be made that the island's ecology and political situation resulted in favorable circumstances which do not exist elsewhere in Latin America.

At the present time, a number of developing countries are planning or have already begun to implement primary health care programs. Pilot projects or demonstration areas are usually established in each country before wide-scale implementation. Many of the primary health care projects in Latin America and the Caribbean are heavily oriented towards the clinical diagnosis and treatment of patients. The clinical facility is static rather than mobile and staffed by lower echelon health workers. Despite attempts at community motivation and participation, underutilization is a problem in some areas. Supervision is a particularly pressing problem which is complicated by evaluation systems which tabulate services provided (number of clinic visits or vaccine doses administered) rather than the effect on the health of the community (decreased notification of disease or immunization coverage). Supporting services necessary for communicable disease control, such as edidemiologic surveillance, diagnostic laboratory services, and vector control are usually inadequate.

The primary health care schemes ostensibly have a communicable disease and epidemiology component. The actual involvement of epidemiologists and communicable disease specialists in the development of these components has to date been limited. Very little serious attention has been given to identifying the communicable disease control tasks to be carried out at the local level. The complexity of these tasks and the assigned level of responsibility will, in their turn, identify the requirements for staffing, training, supplies, logistical support, supervision, and evaluation. Without this input, the various primary health care approaches will have difficulty in dealing effectively with the prevention and control of the communicable diseases of public health importance.

Summary of Current Organization and Administration

In discussing the current organization and administration of communicable disease control programs, the first point to emphasize is that very few Ministries of Health contain an organized activity by that name. The more common pattern is for strong, single disease programs, such as malaria or tuberculosis, to function as separate units. Epidemiology is still considered synonymous with communicable diseases throughout the developing world, and it is in epidemiology units that one finds national responsibility for the miscellaneous communicable diseases. With the possible exception of immunization activities, the national epidemiology program usually has no direct program management responsibility. The major functions of these epidemiology units are to formulate national guidelines for the prevention and control of communicable diseases, develop training material, evaluate surveillance data, and prepare surveillance reports. As mentioned earlier, the national epidemiology unit may have little contact with the categorical disease programs.

It should also be pointed out that there are a limited number of countries in which the traditional communicable diseases have ceased to be a major public health problem. In the Americas, examples would be countries as diverse as Chile, Costa Rica, and Cuba. These countries share such common features as relatively advanced economic development, policy makers who give high priority to health as a social issue, well-educated and informed communities, above average transportation and communication, and easy access to an extensive network of health services. Under these circumstances, the epidemiology unit described above may be adequate.

The control of communicable diseases in these countries, however, is fragile and far from complete. Available data indicate that levels of gastroenteritis, hepatitis, acute respiratory illness, tuberculosis, and most health indicators are still higher than respectable figures in the developed world. Furthermore, communicable disease control programs which are taken for granted in Europe or North America, such as venereal disease or hospital infection control, are usually limited to major population centers. The capacity to respond to epidemics or new problems may also be limited. Further, the more advanced countries rely very heavily on international reference laboratories to confirm or supplement the findings of the national laboratory. The weakness of the peripheral laboratory service is also a significant factor in lack of surveillance information or symptom complex reporting.

The majority of the countries are in a less fortunate situation. In general, the budget for the traditional vertical disease control program is stationary or being eroded as national funds and international support is channeled into primary health care. The vertical disease control effort is losing momentum and, in many instances, the levels of disease appear to be rising. To a certain extent, this can be blamed on failed eradication efforts resulting in the return of malaria or dengue into areas from which the vector had been eliminated and the appearance of the disease in new susceptibles. With the implementation of extended health coverage, some of the increase may be due to increased clinic visits, improved reporting, and community awareness. Certain diseases, such as paralytic poliomylitis, also increase with improved sanitation and the delay of infection in children until a later age.

While the considerations mentioned in the preceeding paragraph may be factors, the indications are that communicable disease control programs are at a crossroads. Further reductions in the level of support for traditional activities can be expected. In addition, there is an increasing trend to take program responsibility away from epidemiology units or individual program managers and incorporate them as one of several service elements in maternal-child health or primary health care. In the Americas, UNICEF, for example, no longer supports malaria programs and will consider support for immunization programs only if they are presented within the context of primary health care. Separate communicable disease control agencies are now running the risk of becoming irrelevant to the operation of their technical programs. The result has been increasing difficulties in maintaining current achievements, failure to react in epidemic situations, insufficient funding to incorporate currently existing technology into the program, less supervision, and reduced morale. In addition, expansion into new control program areas made feasible by new technology (gastroenteritis and acute respiratory infection) is frustrated.

The lack of involvement of communicable disease control staff in the planning and implementation of primary health care projects has been pointed out. This lack of involvement is not confined to nationals. Epidemiologists in multilateral agencies (PAHO/WHO) and bilateral agencies (USAID) have also remained at the periphery. This undesirable situation is frequently attributed by health planners to the hostile attitude of disease specialists who are inflexible, suspicious of any change which might reduce their authority, and eager to preserve the status quo. The health planners, in turn, might be accused of lack of awareness of the complexities involved in a well-conceived communicable disease control program and a bit reluctant to confront the possibility that many control activities could not be accommodated within the primary health care structure. The situation might best be summarized by saying that the health planners did not ask the advice of the communicable disease specialists and the epidemiologists have been slow to volunteer.

Strategies for the Future

The first question to be answered is whether a communicable disease eradication effort can be justified in the future. Smallpox may well be the only disease whose epidemiology made it a prime candidate for global eradication. Global eradication should be distinguished from elimination of the disease in a region, country, or isolated geographical area, such as an island. Eradication is also a relative term. Human transmission of smallpox has been eliminated, but the WHO has no immediate plans to destroy the virus which will be stored in up to four collaborating centers for an indefinite period for research and reference purposes. Administrators have also expressed the view that an eventual goal of eradication has important program benefits. In effect, by aiming for 100%, 90% may be achieved. Were the target set at the actual goal, only 80% might be reached. Finally, the attitude of the medical humanist that no level of disease should be tolerated is sometimes expressed as the ideal of eradication or "stamping out" a disease.

On balance, eradication does have a place in future strategies so long as the term is carefully defined and not used promiscuously. The smallpox program has, after all, proven that scientists can, under proper epidemiologic circumstances and with the appropriate technology, deliberately exterminate a disease agent. Further technical developments and improved mathematical modeling will eventually force epidemiologists to reevaluate the prospects for global eradication of selected diseases. It is also feasible to consider eradication of several diseases from certain geographical areas.

This may be an island situation like Granada where malaria transmission has recurred or a more ambitious scheme, such as the repeated success of Brazil in eliminating imported foci of Aedes aegypti in that vast country. The extraordinary effectiveness of penicillin against yaws and the low transmissibility of the infection may make regional eradication efforts feasible. In the case of Aedes aegypti eradication, the consensus is that adequate funds and a commitment by all countries of the Americas rather than technical factors stand in the way of a serious eradication program. The appearance of denguehemorrhagic shock syndrome in the region or the reintroduction of dengue fever into the United States of America could rapidly change current attitudes and priorities.

There are also special circumstances where national health authorities should consider continuing traditional vertical programs. Such programs, for example, should be retained in rural or isolated areas in which they may be the only health service available to the population. These programs are also more adaptable to diseases in which the appropriate control measures would be difficult to carry out through the primary health care system. Prime candidates would include environmental sanitation and vector control activities. Vertical programs are also easier to justify when disease levels are high and an intensive, well-supervised effort is required for a definite period. Once disease levels are reduced, the program should attempt to broaden its base to include other diseases with a similar epidemiology.

The combination of related communicable disease control programs is now being undertaken or considered in a number of countries, usually without a great deal of fanfare. The mobile strategies of traditional programs frequently included a multidiscipline team which would attack two or more diseases on a single visit. The tasks performed, however, were those of the individual programs. The present attempt is a more serious effort at integration. Brazil, for example, is experimenting with the integration of the malaria program with immunization, leprosy, plague, Chagas' disease, and Aedes aegypti eradication in selected areas of the country. The acceptance of the fact that multiple vaccine antigens can be effectively administered simultaneously has allowed national immunization programs to quietly begin immunizing children in a more effective fashion with simplified schedules. Periodic mass immunization campaigns are also being abandoned in favor of a strategy of completing the primary series in the first year of life. In other instances, a combination of programs is being achieved by changing the emphasis from one particular disease to a function (e.g., immunization, vector control) or diseases with a similar epidemiological pattern or clinical presentation.

The combination of closely related programs, however, does not assure that integration or even effective coordination will be achieved. Rarely, for instance, can one disease program incorporate a second disease program without significant changes in field operations. Intelligent decisions can be made only when the epidemiology of both diseases is well-known and the limitations of control measures are appreciated. In the past, the impact of control measures directed at one disease against other diseases was appreciated only after the fact. The classical example was the disappearance of new cases of leishmaniasis in some areas following effective malaria house spraying with residual insecticides because of the close proximity of the responsible sandfly vector to human habitation.

When integration of separate programs is not undertaken on a rational basis, some of the undesirable effects of business takeovers emerge. This may be of particular concern when one of the programs is the stronger partner and the epidemiology of the diseases is so dissimilar that common diagnosis and control measures will prove difficult. In such situations, the chief administrator of the dominant program remains in charge and the technical guidelines and field procedures are tailored to fit with those of the major disease. As the budgetary resources will be limited and the director's interest will remain in his special disease, elements of control for the second disease which cannot be incorporated may be reduced or eliminated. If the chief administrator wished to acquire the second program to increase his own staff and budget, the smaller program might cease to exist as a functional unit.

In practice, meaningful integration (rather than combination) may be difficult to achieve for several reasons. Epidemiologically, only a limited number of diseases will meet the necessary criteria. The logistics of integrated field operations may prove exponentially rather than doubly difficult. It will also be extremely difficult to retrain disease specifie field staff unless the tasks to be carried out in the integrated program are well-defined and disparities between the two staffs are reduced to a minimum in prestige and salaries. Reporting, epidemiologic surveillance, and laboratory services will also have to be integrated before the reorganized program is implemented. Program combination is frequently adopted in order to achieve cost reduction and budget projections for both programs may underestimate the real operating costs.

Mere combination of communicable disease control programs is little more than administrative reorganization but may be justified on non-technical grounds whenever shared common services, communication, and transport will result in improved efficiency. Integration of the technical elements of programs, however, should not be undertaken without careful planning, epidemiological studies of the diseases and demonstration areas to prove the feasibility of the concept and "shakedown" unexpected difficulties.

Given these obstacles, which communicable disease control programs should be considered by international agencies and developing countries for integration? The first group might be diseases which have a similar clinical presentation. Examples would include the enteric diseases (including intestinal parasites), tropical skin diseases (leprosy, yaws, superficial fungal infections, leishmaniasis, onchocerciasis, and possibly venereal diseases in rural areas), and infectious ophthalmic conditions (trachoma, onchocerciasis). A second approach would be diseases which have in common a similar diagnostic procedure and laboratory examination. Examples would include the skin scraping/snip of the tropical skin diseases, stool examination for the enteric organisms, acid-fast smears (leprosy and tuberculosis), or the simplified laboratory technology through which a fingerstick specimen of blood, previously utilized only for a malaria peripheral blood smear, is available for serologic tests for a variety of diseases. The third category of diseases would be those with similar control measures, such as prophylactic or chemosuppressive drug therapy (malaria, yaws), immunization, vector control (malaria, leishmaniasis, filariasis). A special category would be the zoonoses for which the Ministries of Health and Agriculture often share responsibility (rabies, hydatid disease, brucellosis). Rather than integration, it would be more proper to consider sharing of resources and promoting intimate coordination among the programs.

If the integration of single communicable diseases is so difficult, is the avowed and often stated policy of integration of communicable disease control into the primary health care infrastructure overly ambitious? The dilemma confronting developing countries is clear. On the one hand, they cannot economically and administratively afford the luxury of increasing numbers of vertical programs with separate demands for money, staff, facilities, and laboratories; on the other hand, demonstrated successes in the design and implementation of integrated programs is limited to special situations and circumstances. The plain fact is that communicable disease epidemiologists do not have sufficient practical experience to advise government on the incorporation of these elements into primary health care.

It is important to distinguish adoption of the policy of integration with effective implementation of that policy. A number of Latin American and Caribbean countries have adopted the policy of integration with no discernible effect upon the day by day operation of either communicable disease control activities of clinical services. Several countries have made administrative changes as a prelude to integration. Colombia, for example, has recently assigned responsibility for national programs in immunization, tuberculosis, leprosy, and sexually transmitted diseases to the division of medical care. Several years will be required before a judgment can be made if such changes at the central level can be translated into the provision of integrated services which have an effect on disease levels.

The majority of communicable disease control specialists are now willing to accept the premise that integration of communicable diseases into primary health care services is a worthwhile objective. Considerable, effective integration can be achieved if the task is approached in a responsible, scientific fashion. An important first step will be for communicable disease epidemiologists and health planners in each country to agree on which diseases are essential elements of the primary health service scheme. While the conferees can assume that gastroenteritis, acute respiratory infections, and childhood diseases preventable by immunization should be included, the process should not be limited to sessions at the conference table. Statistical data on the individual diseases will be insufficient for sound decisions and it may be necessary to secure additional information through special surveys.

The second step will be to determine to what extent the primary health care services are prepared to adopt a preventive rather than treatment strategy. The decision is critical for three reasons. The first is that treatment of the already ill will have very little effect on the actual level of communicable diseases in the community. Curative services alone will also have only a minor impact on the complication, death, and economic loss caused by communicable disease. The third reason is that primary health service systems in developing countries which give higher priority to the open-ended demands for curative services will find it difficult to provide support for essential preventive services.

Future progress will depend on results obtained through limited field studies of combining programs at the local level. The health planners will have the primary health service scheme they have developed; the communicable disease control specialist, his technical knowledge of the epidemiology of the major diseases and the possible control measures. Theoretical discussions will not substitute for the experience gained in dealing with an actual community of citizens, health care providers, health educators, and locally available resources.

Since previous experience has shown that fixed facilities rarely attract patients in sufficient numbers to affect control and will not be adaptable to environmental or vector control activities, the greatest importance should be given to developing effective techniques for community mobilization and outreach activities. An effective referral system to more sophisticated facilities should also be developed. The demonstration area will also have to come to grips with the paradox of the primary health care worker. Briefly put, the paradox is that the least well-educated, lowest paid member of the health team is asked to carry out a multiplicity of tasks which many fully qualified physicians would not attempt.

The critical issue in the integration of communicable disease services will be the identification of tasks appropriate for the multipurpose, clinic-based primary health care worker and those essential communicable disease control tasks which must be assigned to more mobile health auxiliaries. It must also be determined to what extent the clinic worker can participate in these outreach activities. Adequate supervision will be necessary for both fixed and mobile activities. Appropriate training material will be needed for both the primary workers and their supervisors. Effective communicable disease control will also require a single surveillance system which will, for the most part, be symptom based. If feasible, the primary health care workers themselves and certainly the immediate supervisors should be responsible for the tabulation and initial evaluation of the data. The incorporation of simplified laboratory techniques and access to supporting diagnostic facilities should also be carefully considered. It is probable that the clinically-oriented primary health care worker will be unwilling or unable to carry out these laboratory techniques and laboratory auxiliaries may be required.

One of the hallmarks of vertical communicable disease control programs was their emphasis on strong supervision, a built-in evaluation system, and insistence that as many of the evaluation indices as possible reflect the status of the disease in the community. Few primary health care schemes under consideration or in operation have placed sufficient emphasis in these areas. Strengthening in these areas would be a major contribution by communicable disease workers to the primary health care movement. Indeed, it may be possible to adopt the rates of selected communicable diseases or immunization coverage as essential evaluation tools for the general program.

The accumulation of this practical experience may take several years; but once accomplished, it will facilitate the realistic calculation of the logistical support, manpower requirements, and cost of larger programs. Areas in which further operational studies or applied research are needed will also become apparent. There are a large number of primary health care pilot projects already in operation or in the planning phase and implementation of this approach will depend more on human factors, such as a spirit of cooperation, than the need for additional funds. The further these primary health service schemes progress without adequate technical input from communicable disease specialists, the more difficult it will be to affect modifications which become necessary at a later date. Given the predominance of communicable diseases in the tropics, the absence of an effective communicable disease control element may eventually produce disillusionment with integrated health concepts on a scale which may eclipse that which we are presently experiencing with the concept of eradication.

Conclusions

Integration of communicable disease services into the primary health care infrastructure is not only desirable, it may be essential for the developing world. With current knowledge and technology, new eradication efforts are not feasible and poor countries cannot afford a proliferation of autonomous vertical programs. The participation of communicable disease epidemiologists in the development of primary health service schemes has been disappointing up to the present. As a result, the communicable disease element of these proposals is inadequate.

Complete integration at the national level will probably not be realistic because of the need for the expertise of specialists at this level. Integration at the local and regional levels will be hampered by the lack of information, insufficient trial and error or communicable disease control strategies in the field, and the orientation of primary health schemes towards curative medicine rather than primary prevention. Primary health care pilot projects and demonstration areas are currently being funded in many developing countries. Highest priority must be given to developing the appropriate field technology for communicable diseases within these projects in preparation for extending integrated health care systems to larger areas.

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SURVEILLANCE

by

Stanley I. Music

To an epidemiologist, surveillance is a process, an activity. Surveillance is how one learns what is happening. Surveillance takes the pulse of the community. In epidemiologic parlance, an epidemic or outbreak exists when the observed number of cases of a given disease exceeds what is expected and is associated with a common or propagated source of infection. Surveillance is the process by which one obtains information to make this comparison.

As an organized public health activity, systematic surveillance may be defined as "...the continuing scrutiny of all aspects of occurrence and spread of a disease that are pertinent to effective control." The practice of surveillance can be arbitrarily divided into three distinct elements:

systematic collection of pertinent data,
analysis and evaluation of the collected data,
prompt dissemination of relevant information to persons who need it.

In practice, these three factors are a continuum and constitute an internal feedback loop. The third component is often mistakenly undervalued and may even be ignored, though not for long without penalty. One cannot expect to receive information from others unless their efforts are seen as useful and rewarding. Probably the single most important factor in the demise of surveillance systems is lack of meaningful feedback to the sender/source. Personal communication is a vital part of all surveillance; the core or essence of surveillance is people interacting with people about human disease. Interaction is inhibited if allowed to become unbalanced or excessively unidirectional.

The Value of Surveillance

The value of surveillance can be illustrated by an Army Corps of Engineers project called Malaria Control in War Areas (MCWA). It was designed to keep people and mosquitoes away from each other by draining swamps in the southeastern United States where many troops were being trained after the United States entered World War II. Malaria was a concern in many southern states since thousands of cases were being reported annually and the importation of quinine had been compromised by the war. Malaria prevention seemed a very reasonable approach. When some of the project resources were ex-

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pended on malaria surveillance, tracking down cases, and defining the basic epidemiology of malaria in the region, the engineers on the project objected strongly. They thought that surveillance was a waste of time and money. However, the surveillance was pursued and some amazing things were soon learned. Most cases of malaria could not be confirmed by blood slide. They had been reported by long-established rural physicians who diagnosed malaria on the basis of clinical presentation alone--fever with or without a palpable spleen that occurred at the "right" time of year. Malaria confirmed by blood slide uniformly occurred in people who had been overseas in known malarious areas and had returned while incubating the infection or in people who had previously had malaria. It was obvious then that indigenous transmission of malaria had ceased in the southeastern United States before inception of MCWA.

Hence, it was shown that if surveillance had been the basis for administrative decisions in the establishment of a disease control program such as MCWA, it would have been discovered earlier that malaria was not a problem. The incident just described is a classic example of the use of surveillance to evaluate program effectiveness.

Surveillance then is a tool that may be used in developing as well as in developed countries to tell health authorities what is happening and to permit effective disease control, program planning, and evaluation.

Kinds of Surveillance

Historically, many kinds of surveillance systems have been attempted and found useful in varying degrees for irregular periods of time. Generally, they have either been phased out or they evolved into systems which are in use today throughout the world. All surveillance has three components: the surveillance information itself, the sender/source, and the gatherer/recipient.

From the viewpoint of the gatherer/recipient, surveillance can be either active or passive. In passive surveillance, the sender/source acts as a "donor: and submits information about disease occurrance to the gatherer/recipient. The recipient is entirely passive and is dependent upon the sender/source's initiative for receipt of data. The recipient expects to receive reports/information, usually because the sender/source is "required" to do so. Most of the formal or ongoing surveillance systems in existence at this time are of this type. A law or regulation is promulgated stipulating some facility or person (physician, hospital, administrators, local health officers, etc.) as sender/source for information to be sent to a gatherer/recipient.

Experience has shown that passive systems work best when a negative report is required, i.e., the sender/source is required to report even when there are no cases. The system tends to fail when only cases are reported. Under such circumstances, the recipient has difficulty interpreting a lack of a report since it can mean either no cases or noncompliance.

Active surveillance turns the recipient into a gatherer, responsible for getting the information by actively searching and looking for cases. The gatherer is not passively dependent on sender/source. A prime example of this is the WHO Smallpox Eradication Program that energetically searched for smallpox cases by sending surveillance teams on regular schedules into all areas of every country in the program and provided incentives to the populace for reporting cases of smallpox.

Relative to time, surveillance may be either prospective or retrospective: events may be monitored as they actually occur (prospective) or events may be reconstructed in order to determine what happened in the past (retrospective). It is commonly taught that prospective epidemiologic studies are less subject to bias and, therefore, more accurate than retrospective studies. Bias, of course, can occur in any study, and each mode of ascertainment has unique characteristics that can be used advantageously in varying circumstances.

It is important to understand the characteristics of active, passive, retrospective, and prospective so that surveillance systems can be designed to meet circumstances and the needs of those who need to know what is happening.

Surveillance systems may be based on mortality data or morbidity data. Again, each has its characteristics, advantages, and disadvantages. Whereas it is easy to miss cases through morbidity surveillance, i.e., cases of disease may go undiagnosed and unreported, mortality surveillance has the advantage that death is relatively unequivocal, finite, easy to recognize, and more frequently reported. While a much larger proportion of deaths is reported than cases of virtually all nonfatal disease, both morbidity and mortality data have problems of diagnostic accuracy. Legionnaires' disease is easy to mistake for viral pneumonia. Cholera may be indistinguishable from other diarrheal diseases without special bacteriologic tests. Typhus and typhoid are still being confused.

Surveillance systems may also be related to specialized health facilities or services which serve as axes or pivots around which surveillance can be conducted. Clinics, hospitals, and laboratories--virtually any focus of health activity--can be used as a surveillance-gathering center. Hospitals and clinics are the obvious ones and most countries keep some records and have reports sent from local areas to central organizations with the numbers of patients and diseases that are seen. Much of this surveillance, however, is of the routine archival type: the information is usually collected unenthusiastically and utilized in an uninnovative way. When a hospital or government laboratory provides a service such as rabies diagnosis or syphilis diagnosis, it becomes relatively easy to followup on the requests for service and to begin to get an idea of the epidemiology of the particular disease for which this service is sought. In fact, the community at large is much more responsive to requests for information about disease occurrence when it perceives that it receives a service in return. Whether that service is laboratory, epidemic investigation, or simply equipment provision, such as immunization materials, the rate at which these services are requested or utilized is an indicator of what is happening in the community at large.

General Comments on Surveillance

Much of the current, formal surveillance throughout the world uses physicians as primary informants. This is logical because physicians make diagnoses, and it is upon diagnoses that most surveillance systems are based. However, physicians frequently are not very satisfactory sources of information. The teaching of epidemiology and surveillance methods has a low priority in medical schools throughout the world, and most physicians and paramedical personnel are not trained to think of disease in terms of population rates or in community assessments. Physicians are oriented towards individuals, towards the alleviation of suffering, towards after-the-fact so called "curative medicine." Most physicians are not public health oriented and often fail to see the need or the usefulness of reporting accurately or quickly to central public health authorities. Curative physicians sit in hospitals or offices and wait for people to come to them to apply their medical skills. The public health doctor is different. He cannot sit behind a desk and expect that the community will come to him when it has a problem. He must go out to learn what is going on in the community. In short, he must look for indicators of disease in the community.

This manual is composed of papers on specific disease control methods for developing countries. Each disease has one or more indicators that suggest to the knowledgeable the existing level of disease. Fundamental to all disease control activities are baseline data which indicate how many people live in an area or region, their geographic location (by administrative or reporting unit), and some disease and death information by sex and age groups. This information provides some idea about how people in the area under study live and die, and what diseases affect the quality of their lives. If the disease of interest is poliomyelitis, a useful indicator might be the rate that asymmetric paralysis can be detected in the population. If the concern is smallpox, a useful indicator might be the rate that compatible scars occur on the face or individuals in certain age groups. If smallpox was eradicated 15 years ago in a given country, then smallpox scars should not be present in anyone younger than 15 years of age in that country. A knowledge of the epidemiology and methods of control for the disease of interest will suggest indicators that are useful in studying its prevalence and severity.

The surveillant must approach the community with a different mental attitude than the curative physician. The public health epidemiologist must be flexible, innovative, and able to get as much information as possible from the resources at his/her disposal. All surveillance systems cost something in terms of money, personnel, and effort. Such resources are scarce and should be used carefully. The expenditure of resources on surveillance of diseases for which no control measures exist is an academic exercise of little value. It would be of little use to be very comprehensive, very accurate, or to expend a lot of effort on a system designed to report baseline data when nothing could be done about a situation.

Surveillance can be accomplished at any place, at any time, and with whatever resources are at hand. It is not necessary to have an elaborate system or to wait until "everything is ready" in order to begin surveillance.

It is probably not a good idea to try to find all cases. Complete reporting is expensive, time consuming, and usually provides little more information than incomplete reporting. A random sample survey of the population or medical care providers can give an accurate picture of disease occurrence and its distribution. As long as those engaged in surveillance have some idea of the proportion of actual cases reported and their distribution, incomplete reports will be quite adequate to delineate important characteristics and disease patterns, such as age distribution of cases, seasonal cyclicity, increasing or decreasing total number of cases, among others.

Feedback is an essential ingredient in keeping surveillance systems going. However, simple publication of reported cases of a given disease is insufficient feedback to the reporting source. Interpretation of collected data is feedback:

(1) definition of the current situation;
(2) discussion of trends and changes;
(3) improvement or decline in specific diseases by geographic area or region; and
(4) what it all means.

Data interpretation is the practicing epidemiologist's constant activity: it is the interpretation that must be put into clear, ordinary language and sent back to the sender/source.

Improved surveillance generally results in an increase in reported cases of a disease. Any sharp rise in reported cases should be first scrutinized to detect reporting artifacts before being accepted as genuine. Unexpectedly enhanced reporting may create difficulty. As the number of cases begins to rise, officials in the central ministries often get disturbed because they think a new epidemic has begun. If made aware that the number of cases is going to rise because of improved surveillance, central ministries will not become alarmed.

An Example from the Developing World

The author recently had an opportunity to observe and to assess the surveillance system (or the lack of a surveillance system) in an Asian country. This developing, industrial country began an ambitious program of economic development 16 years ago. That program has been an unprecedented success: it transformed a marginally sufficient, rural, agricultural subsistance economy into a rapidly emerging urban, industrial, and technological economy which is self-sufficient in food and capable of burgeoning commodity exports.

Health, in the sense of government programs, has never been a priority and has, in fact, been labeled an unaffordable luxury until such time as the country might develop sufficiently and appropriately. In the first three Five-Year Plans (1962-1976), the Ministry of Health and Social Affairs (MOHSA) received only about 0.5% of the total government budget. Essentially all resources and talent were funneled into economic development and national defense. The fourth Five-Year Plan (1977-1981) marks the first time the government made health a priority by increasing the health budget by 450 percent.

Health activities in the public sector are fragmented and divided among several ministries: MOHSA and the Ministry of Home Affairs have the major responsibility and authority. The Ministry of Science and Technology and the Ministry of Education also play important roles, however.

This cutting up of the "health pie", from a managerial point of view, has some unique characteristics. The people who set policy are very many levels away from the people who deliver health care and who see the practical problems encountered in program implementing. Because whole ministries are involved, some sense of competition or territoriality between ministries has been created.

Though MOHSA is responsible for health, it appears to have little authority. All personnel in the public medical sector--from the provinces down to the health subcenters--are supposed to take their technical direction from MOHSA, but they are under the administrative authority of the Ministry of Home Affairs. Each ministry is able to know only a part of the total health picture. Duplication and competition do occur. And three of the four ministries involved in health have continuous ongoing non-health programs which, in general, are of higher priority than their health component.

The country does not have a central agency which is really capable of coordinating national health data with other information. Such statistics as do exist are often inaccurate and/or inappropriate for planning. The usual indicators, life expectancy, birth, infant mortality rate, etc., are useful for comparing this country to others and for internal monitoring as a crude index of progress. However, such indicators are much too insensitive for planning, since they cannot be directly related to specific causes of disease problems. Even statistics obtained directly from health programs are not particularly well adapted to planning purposes. For example, a national immunization program aimed at controlling vaccine preventable diseases is a corner stone of the country's preventive medicine activities. Yet immunization statistics in this country specify only the number of doses dispensed for each vaccine. It is not possible to know how many children received their scheduled immunizations; how many remain susceptible; or even to identify which areas have lower immunization rates than others--all common indicators elsewhere. In this instance, the simplest statistic, a measure of activity rather than effectiveness, has been accepted as the desired data. This type of health data has little relevance in areas where scarce resources must be allocated intelligently and have maximum health benefit.

The private sector--where most of the medical care is actually delivered--contributes the least reliable and smallest quantity of health information. This is true for the private sector in almost all countries, but is a special problem in this country for the following reasons:

> Traditional healers or the ubiquitous pharmacist are the major source of medical care, and they do not report.
>
> Clientele of licensed physicians are predominantly urban and upper-class, a biased sample from which reporting might be available.
>
> A virtual absence of reliable diagnostic laboratory services forces most private physicians to make diagnoses on the basis of clinical impression.
>
> Physicians are reluctant to report officially what they merely suspect.
>
> Reporting of highly contagious diseases particularly is discouraged by regulations which require mandatory isolation at specified facilities which are held in low public esteem.

It is important to note that even if these special problems were solved, passive reporting from the private sector has never--in any country--been able to provide to government an adequate data flow for purposes of health planning. Private physicians are not public health or preventive medicine trained or oriented: their ability to recognize public health problems is severely compromised and almost non-existent.

The governmental public health establishment also has difficulties. Its main public health concerns are the exotic, acute, seasonal infectious diseases that attract attention in the press and are, therefore, "sensitive". It is characteristic, under such circumstances, for the whole public health establishment to be defensive, reluctant to publicize problems and to minimize the problems that do surface.

In general, the overall disease burden is smaller now than at any time in the country's more than 4,000 years of recorded history. While it is likely that a dramatic decline in human disease has taken place in the last 20 years, this conclusion must be qualified in at least two important ways: (1) only circumstantial evidence but no hard data exist to support this statement. The decline in morbidity and mortality is not uniform; it has occurred, to a greater degree, in urban rather than rural areas and for some but not all diseases. (2) Some diseases may actually be increasing. Chronic disease problems characteristic of urban industrial populations which contain a large proportion of elderly persons are beginning to be noted. The full effects of the country's massive air and water pollution will not be apparent for many years.

The country does not yet have an effective working group of physician epidemiologists. To be sure, there are a few good epidemiologists in the major medical schools, schools or public health, and the National Institute of Health. But, there is nobody whose fulltime job is disease surveillance, merging and analysis of data, or responsible for effecting control measures. The lack of working epidemiologists probably accounts for most of the problems of coordination and proficiency in this country's public health services. While there is a growing awareness of the health benefits which may be derived from economic development and the deficiencies in the health data system discussed above, there is also a consensus that the system should be changed. This consensus exists throughout the medical field; in the public, private, and academic sectors.

With proper surveillance and reliable data, it would be easy to know what the real health problems of the country are. No one today knows what the leading causes of death are, or what diseases take the greatest toll on life and economic productivity. There is now no rational public health or economic basis for assigning priorities to competing health programs.

The country would benefit from the creation of a national health data and information capability. Actually, many components of such a center already exist and need to be reorganized and given augmented support to become functional for the purposes of disease surveillance, control, and health planning. What is missing is a corps of trained epidemiologists to tie the complex, overlapping system together to make it work. The formation of such a group of epidemiologists has been recommended.

Conclusions and Recommendations

Any surveillance system should be designed for a specific country and situation. It should be done by local people according to their own values and their own cultural preference. Proper and appropriate surveillance can assist any country to obtain health planning information so that it can see its own problems and start its own course in the public health field. Health planning and disease control is itself a developing field: no country has the perfect system. No existing foreign technology can or should be transplanted directly into any country. Each country should find its own solution to its problems. The world at large will benefit from each country's entry into public health planning on its own terms. We all have much to learn from each other.

With appropriate surveillance, the following should be possible:

Identification of health problems which have cost-effective interventions and the highest priorities.
Calculation of the cost benefit of one public health program versus another competing for the same resources.
The ordering of meaningful priorities in medical research, preventive medicine, and/or health care delivery.
The evaluation of the effectiveness of current expenditures to reduce disease burden.

Each country really needs a corps of trained epidemiologists to set up surveillance systems and to perform necessary tasks in this essential field of public health. Epidemiologists should:

(1) have a mandate to pursue actively the collection and interpretation of all relevant health information;
(2) have a location in government that ensures easy access to all ministries at all levels involved in health;
(3) be an advisory consultation and support service to all private and public medical establishments at all levels;
(4) be nonregulatory and nonpunitive;
(5) be a national resource for information and experience in disease surveillance and disease control;
(6) have the authority to provide health data to those who need it and in a form which can be used;
(7) have an attractive career and salary structure to assure that this vital function is performed by the best possible people.

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IMMUNIZATION PROGRAMS

by

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Health improvement in the developing world requires a wide range of preventive and curative health programs. Ministry planners and consultants are usually challenged with a large number of options for the use of limited resources. Among possible program options, mass immunization programs have been shown to be one of the most effective and least expensive preventive health measures.

During the last few decades, immunization usage has increased as has vaccine quality and stability; delivery has improved and public acceptance has widened. This paper discusses the major issues involved in the planning and evaluation of multiple antigen immunization programs in developing countries.

Planning decisions require a basic knowledge of in-country demographic and morbidity data, an understanding of cultural and logistic variables, sound technical knowledge, and an ability to predict technical and logistic feasibility. Key steps in the planning process include:

Identification and quantification of health needs.
Identification of possible key areas of intervention.
Assignment of priorities.
Identification of specific time-phased quantitative objectives.
Design of work plan including task analyses and job descriptions.
Evaluation.

For programs that involve external assistance, three additional considerations are important:

Compatability of program with other health service programs.
Potential of project to significantly improve national capability to deliver health services.
Reasonable withdrawal of external assistance which maximizes national capability to continue program.

Data Evaluation

Development of a reliable data base on which planning can proceed is essential. Most governments collect and publish annual summaries of disease and service statistics, though often delayed 3-5 years. Available data is often limited to that collected from major

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facilities in urban areas and may have little relevance to rural populations. First priority should be assigned to the evaluation of the representativeness, comprehensiveness, and accuracy of the available data. Basic questions that need to be asked include:

1. Who is doing the reporting? (Facilities and Individuals.).
2. What is being reported? (Type of disease and services being reported).
3. When does reporting occur? (Weekly, monthly, annually).
4. Where are reports being generated? (Distribution by geographic area and type of facility).
5. Why are reports submitted? (Are reporters motivated by a purpose, or are they performing what they consider a meaningless clerical task?)

The surveillance system cannot be fully understood by what is seen and heard at a central health ministry office of statistics, but requires field evaluation of reporting channels at intermediate and peripheral levels.

Understanding what is and what is not reported and why enables a consultant to evaluate the adequacy of current data as well as the necessity for and feasibility of collecting additional data. Sample surveys of reporting completeness have shown variations in reporting for different diseases ranging from .01 percent to 10 percent within the same system. Factors which affect the completeness of reporting include:

Probability of infected person realizing that he is ill.
Probability of ill person seeking medical care.
Probability of person seeking care making contact with health provider.
Probability of diagnosis by history and clinical examination.
Probability of diagnosis by laboratory (if facilities available).
Ability of service provider to make correct diagnosis with facilities available.
Probability of disease being recorded at facility level.
Probability of report being cumulated and dispatched.
Probability of report reaching central level.
Probability of reports being collated at central level.

In addition to data available from existing reporting systems, other sources of data may also be utilized.

Demographic Data: Demographic data may not be available within the Ministry of Health. It is important to explore other potential sources of data, such as:

Government ministries-census, planning, economic development, agriculture, education;
Universities;
International agencies;
Bilateral agencies.

Health Data: National institutions-development projects, health projects; international agencies; voluntary agencies.

Cultural Information: As effective health program development requires both provision of a service and public utilization, adequate programming requires an understanding of local cultures and values. Information should be collected on development projects,

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cooperatives, local political organizations and universities.

Only after a thorough review of all available data can a judgment be made as to whether or not sufficient information for planning purposes exists.

Quantifying Diseases Preventable by Immunization

For planning purposes the required amount and accuracy of the data varies by disease. While it is essential to know about a single case of smallpox, estimates derived from sample surveys are sufficient to plan programs for more common diseases such as neonatal tetanus. Unfortunately, tradition has relied primarily upon a single surveillance system to serve all purposes rather than selective surveillance systems to meet variable needs.

The type of surveillance system needed will depend on disease incidence, the type of information required, the proposed use of the data, and an estimate of the most reliable and economic method of obtaining the data. Examples of approaches to surveillance include:

Reporting from all health facilities: required submission of regular reports from local to central level. Largely from a lack of understanding by the data providers of what is being done with the information and also the absence of feedback, such systems often provide very little useful data. However, high levels of reporting can be achieved through training and two-way communication. For diseases in which detection of a single case requires immediate public health action, e.g., yellow fever, hemorrhagic fever or smallpox, reporting from every health facility is essential.

Sentinel site reporting: requires regular reporting from selected health facilities. Facilities are chosen on the basis of the quality of information available and the willingness of those responsible to participate in the reporting system. Regular feedback to these sites in the form of data summaries and interpretation are important to encourage high levels of performance. Such systems are useful for the surveillance of high-frequency diseases, e.g., measles and pertussis.

Sample surveys: consist of interviewing statistically selected groups of a population about a certain health characteristic in order to estimate population rates. Cluster sampling techniques have been developed in which approximately 10 respondents are interviewed in each of 30 clusters. This type of surveillance is the best method to estimate incidence of neonatal tetanus. Such active case detection may be preferable to reliance upon cases who present themselves to health facilities. For low-frequency diseases, such as poliomyelitis, surveys of school children for residual paralyses may be used to estimate the prevalance of poliomyelitis.

Sample surveys with laboratory tests: utilize skin testing or laboratory examinations in addition to interviews. Tuberculin skin testing, examination of sputum for acid-fast bacilli and serological tests for measles hemagglutination-inhibiting (HI) antibodies are studies of this type.

Prospective community screening: involves longitudinal follow-up of selected population groups. As demonstrated by Morley in Nigeria, long-term surveillance of a selected population may provide accurate assessments of mortality and complication rates associated with measles and pertussis. Although time-consuming and expensive, these studies provide high quality data and are frequently the only way to investigate possible interactions of variables such as measles and malnutrition.

Community search for cases: requires periodic visits on a village-to-village search for cases and on-the-spot treatment is optimal.

Public reporting systems: encourage individuals to report cases of notifiable diseases to appropriate authorities. The Smallpox radication Program has shown the public's inherent ability and competence to recognize suspect cases and participate in reporting system.

Disease-Specific Issues

Morbidity and mortality patterns in developing countries are seldom similar to those experienced in the United States. Even within developing countries, patterns of disease vary significantly with population density, mobility, cultural practices, and climate. The goal of an immunication program should be to prevent disease, not merely to give immunizations. Therefore, potent vaccines must be administered effectively prior to the onset of natural infection. Thus, effective planning also requires a thorough understanding of local disease patterns.

The following summaries emphasize the range of disease patterns existing in developing countries and refer to some of the major issues which still require investigation:

Measles: Although a mild disease in the U.S., approximately 10 of every 100 children born die from measles in areas of West Africa. Mortality results from four causes: the disease itself, secondary bacterial complications, diarrhea, and malnutrition--alone or in combination. Measles immunization programs in dense urban areas of Nigeria, for example, are faced with a serious problem. While the median age of infection is felt to be about 14 months of age, measles cases begin to appear as passively acquired maternal antibody wanes at 8 or 9 months of age. Yet high levels of seroconversion to measles vaccine appear to be attainable only after 9 months of age. Thus, there is no right time to provide immunization. Some countries provide two doses of measles vaccine: the first at 6 months and the second at 12 months. Nine and 15 months might be preferable. Obviously, immunization rounds in these areas need to be conducted frequently. In rural areas, however, measles appears as an epidemic disease that affects children at 24-36 months of age and this gives immunization teams a considerably longer period to adequately protect the target population.

The morbidity and mortality associated with measles in Africa has not been reported from Asia or Latin America. Further study is necessary to clarify the importance of measles in these areas of the developing world.

Although the annual incidence of measles is estimated to be 90 percent of all live births in unimmunized populations of developing countries, the actual significance of measles as a public health problem requires improved measurements of mortality as well as direct and indirect complications of the disease.

Pertusis: Due to diagnostic difficulties, pertusis is not commonly reported. However, it is felt to be a major unrecognized killer of children under 1 year of age in developing countries. The high rate of pertusis agglutinins in children under 1 year suggests infant attack rates of up to 80 percent in certain African countries. The importance of long-term pulmonary and nutritional sequelae is only now being recognized. Pertusis remains a priority problem for clinical, epidemiological, and vaccine-related research.

Neonatal Tetanus: In come countries, neonatal tetanus is the number one cause of infant mortality. Neonatal tetanus may occur in up to 15 percent of all live births and usually results in death. This disease occurs at home primarily and is usually not detected by health facility based reporting systems. The striking nature of the clinical syndrome allows sample surveys to estimate incidence accurately. A neonatal death within 1 month of birth with a history of normal sucking at birth, loss of ability to suck, and evidence of trismus is often sufficient to establish the diagnosis. Neonatal tetanus can be prevented by immunizing women of childbearing age with two doses of tetanus toxoid, given 2 months apart, which protects children born within 3 years.

Poliomyelitis: Poliomyelitis has only recently been documented as a major health problem in developing countries. In countries where a high percentage of children attend school, school surveys for paralysis without sensory changes provide an estimate of the prevalence of residual paralysis. After correcting for mortality and recovery, estimates of disease incidence can be made. As standards of living improve in the developing countries, poliomyelitis can be expected to become a greater problem.

Oral polio vaccines are advantageous in epidemic situations because of the associated spread of vaccine virus among even nonimmunized individuals. Yet the routine use of oral polio vaccine is being challenged by advocates of killed vaccine who cite problems with heat liability, maintaining refrigeration, and low seroconversion rates associated with oral vaccines. Adequately controlled vaccine trials are necessary to resolve this continuing debate.

Diphtheria: Among the diseases prevented by standard antigens, diphtheria is the least understood. Because of high rates of skin infection by atypical diphtheria organisms, noncutaneous diphtheria is not felt to be a major problem. However, in certain countries diphtheria is increasingly being recognized by those who search for it. Additional knowledge is certainly necessary to determine the importance of this disease in developing countries.

Tuberculosis: Tuberculosis provides a continuous challenge to those who are involved in its prevention and treatment. Prevalence of past exposure can be estimated by tuberculin skin test surveys, and active disease rates can be estimated by sputum surveys. BCG immunization at birth has been established as WHO policy in the Expanded Program on Immunization (EPI). Due to variability in strains, the absence of a postimmunization monitor of immunity, and persistent doubts regarding its efficacy, BCG remains a controversial subject.

Setting Priorities

An essential step in the planning process is the use of the available data to establish priorities. For each option, the relative importance and the likelihood of success must be taken into consideration. Frequently, decisions may need to be made without complete information, but the following factors require attention before key decisions can be made in immunization programs: disease

Table I

FACTORS REQUIRING CONSIDERATION IN ASSIGNING PRIORITIES FOR IMMUNIZATION PROGRAMS

A. Disease

- Morbidity (Age Specific)
- Mortality (Age Specific)
- Complications
- Residual Disability
- Communicability
- Geographic Distribution

B. Technical

- Vaccine Potency
- Vaccine Stability
- Vaccine Efficacy
- Number of Doses
- Route of Administration
- Rate of Complication
- Age Range of Susceptibles
- Cost

C. Management

- Authority
- Responsibility
- Manpower Availability
- Monitoring Capabilities
- Transport
- Cold Chain (Supply, Storage, Distribution, Delivery)
- Methods of Vaccine Administration
- Population Density
- Population Accessibility
- Facilities
- Morale

D. Government Commitment

- Planning Priorities Within Ministry of Health
- Resource Allocation Within Ministry of Health
- Epidemic/Endemic Status
- Who Gets Disease
- Cost (Prevention, Cure Disability)
- Press Recognition
- Expressed Public Desire

E. Public Response

- Felt Need
- Access to Services
- Expectations
- Education
- Propaganda (Pro and Con)

measures, technical feasibility, management feasibility, government commitment factors, and public response factors. Table I lists some of the factors which need to be assessed in setting priorities.

Determining Program Objectives and Strategies

Once a list of priorities by disease and by geographic area has been established, the next step is to establish program objectives and design strategies. As these two activities are considerably interdependent, they can be considered a single step. Possible achievements depend in large measure on available resources. Constraints on these resources almost inevitably result in necessary downward revisions of objectives.

A good starting point is a comprehensive statement of the ultimate objective of the immunization program. In many instances, this statement will already have been made, as a part of the country's general development plan or as a Health Ministry plan. If no such statement exists, planners should formulate the general goal before developing short-term objectives and strategies.

The ultimate program objective provides a general picture of the mission and scope of the immunization program. WHO has put forth as the ultimate objective of its Expanded Program on Immunization to reduce the morbidity and mortality that results from six target diseases (measles, poliomyelitis, diphtheria, tetanus, pertussis, tuberculosis) by providing immunization against these diseases for every child in the world by 1990. Individual countries may change the number and/or types of vaccines to be provided as well as the year by which national coverage will be available.

National immunization programs should generally be planned for gradual phased expansion over a 5 to 10-year period. The long-range plans, of course, must be considered tentative and subject to change based on operational experience. However, plans for the first year of the program need to be comprehensive and definitive. The antigens to be given must be selected along with geographic areas and target populations. Next, the immunization delivery strategy (fixed/mobile/outreach) and the immunization schedule appropriate for each strategy must be determined. Then the resources required to implement the program must be estimated and the program revised if available resources are insufficient to cover the cost of implementation.

Once program strategies have been designed, specific and quantitative objectives can be established.

Planners should identify one to three geographic areas for first year operations and, to the extent technical feasible, should include antigens for all of the priority diseases. To maximize chances for successful implementation, selection of geographic areas should be based on the following criteria:

a. The areas should be easily accessible, with extensive and usable road and communications systems;
b. The areas' health services should have a large number of accessible health service centers and dispensaries, a large number of skilled health workers available, and adequate cold chain facilities for vaccine storage and handling.
c. The areas' population should have a history of public cooperation with health programs, and be large enough

to justify the expense of an immunization program.

Selection of Target Population

Depending on the adopted strategy and age group(s) to be included, and the antigens to be given, estimates of the target populations can be made from the best available census and/or demographic data available. For example, in a maintenance program of childhood immunization, the target population is approximately equal to the number of infants who survive to 1 year of age.

There are three basic vaccine delivery strategies:

Fixed strategy: consisting of static clinics or health facilities.

Mobile strategy: consisting of an independent group of health workers that travel to areas where no health facilities are available. This type of program is the most expensive due to the cost of additional personnel, transportation, and equipment.

Outreach strategy: similar to fixed but with staff that travels regularly to subcenters, dispensaries, or villages where no facilities are available.

The vaccine delivery strategy to be used in each area and the selected priority diseases determine the immunization schedule to be used (i.e., which vaccines will be given at what ages). The recommended number of doses for each vaccine is given below:

Measles--1 dose
DPT --3 doses 1 month apart (2 doses 2 months apart may be equally effective)
Polio --3 doses (1 month apart)
BCG --1 dose
Tetanus--2 doses (for women of childbearing age)

Immunization schedules depend on whether the services will be provided by a fixed, a mobile, or an outreach strategy. More time is required by a mobile than a fixed program to administer a full round of immunizations due to the large amount of time spent traveling to multiple sites in a mobile program.

The following are sample immunization schedules by age and type of vaccine for fixed, mobile, and outreach programs.

Fixed Schedule:
- 2 months--1st DPT, BCG, 1st Polio
- 3 months--2nd DPT, 2nd Polio
- 4 months--3rd DPT, 3rd Polio
- 9 months--Measles

Mobile Schedule:
- 3-8 months--1st DPT, BCG, 1st Polio
- 9-14 months-2nd DPT, 2nd Polio, Measles
- 15-21 months-3rd DPT, 3rd Polio

Outreach Schedule
- 2-4 months--1st DPT, BCT, 1st Polio
- 5-7 months--2nd DPT, 2nd Polio
- 9-14 months-3rd DPT, 3rd Polio, Measles.

The resources required to implement an immunization program can be divided into three major categories: personnel, material, and operating costs.

Personnel considerations include the following: identify all personnel needed. Identify personnel currently working in the country's health system whose duties can be changed or expanded to include immunization. Identify other personnel (nongovernmental) whose duties can be changed or expanded to include immunization. Determine additional personnel needs (personnel to be hired). Determine annual personnel costs including salaries (full or part-time, by category) and allowances.

Material concerns include: Identify all material needed. Identify material currently available in the country's health system which can be used for the immunization program. Determine additional material to be purchased. Determine total material costs for first year.

Determine the total operating cost by multiplying the annual operating cost of each item times the number of items in operation. The total first year cost of the program is computed by adding perconnel, material and operating costs. Then, funds required are compared with the funds available from the health budget. If available funds are sufficient, the planning process may continue and specific objectives may be established. If, however, abailable funds are insufficient, the program must be modified or additional resources must be obtained.

After the first year program strategy has been designed, first year program objectives can be established. The objectives should be established on three levels.

First is the number of people to be immunized. The target population was already identified when program strategy was designed. Although it is operationally impossible to reach 100 percent of the target population, this figure can be used as the number of people to be immunized unless a better estimate can be made.

Second is the number of people expected to become immune. Since vaccine efficacy is always less than 100 percent and since not all of those who receive vaccine will be susceptible at the time of immunization, not all of those immunized can be expected to become adequately protected.

To estimate the number who become immune, the following formula may be used:

No. of People to be Immunized X % Susceptible at Time of Immunization X Vaccine Efficacy Rate = No. of People Expected to Become Immune

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Generally accepted values for percent susceptible and vaccine efficacy rates are provided below:

VACCINE	DOSE	ESTIMATED % SUSCEPTIBLE AT TIME OF IMMUNIZATION	ESTIMATED VACCINE EFFICACY RATE (%)
Measles	1	60-90	95
Polio	3	50-80	80
Diphtheria	2 or 3	95	95
Tetanus	2 or 3	100	95
Pertusis	3	60-80	80
BCG	1	100	Up to 80

The reduction in morbidity and mortality expected to result from the number made immune should be made an objective. These will be the most difficult objectives to establish and to measure. They will need to be revised as surveillance improves and may be considered crude estimates until the program has developed.

In order to establish these objectives, the following must be known or determined for each disease: attack rate, number expected to become immune, cases prevented, case fatality rate, and deaths prevented. This information may be recorded/determined using the following worksheet:

REDUCTION OF MORBIDITY AND MORTALITY (YEAR 1)

(1) Area	(2) Disease	(3) Attack Rate	(4) Number Expected To Become Immune	(5) Cases Expected to be Prevented (Col.3 x Col.4)	(6) Case Fatality Rate	(7) Deaths Expected to be Prevented (Col.5 x Col.6)
TOTAL						

In attempting to follow this process, countries may encounter problems. For instance, attack rates may be unavailable. If so, the initial phase of the program should be planned so as to obtain information on attack rates. It may be possible to do so by improving the surveillance system. In the meantime, countries should use the best available estimates or information from similar areas.

Initially, cases are also likely to be underreported. As surveillance improves, more cases may be reported. This should be anticipated and should not be taken as evidence that cases are in fact increasing.

Despite the problems, it is essential to establish morbidity and mortality reduction objectives. Only by focusing on the reduction of disease can an immunization program demonstrate its effectiveness.

Planning for a nationwide program will be a multi-step process. Tentative plans for a 5 to 10-year program can be made based on priorities established in terms of disease, funds available, and program costs. These plans should then be revised based on an evaluation of the first year of the program and should be annually revised based on new information. Expansion into a nationwide program may occur gradually. The rate of expansion will depend on available funds and available information on program effectiveness. Final plans for a nationwide program should consider the following factors:

The successes of the first year of the program;
The failures of the first year of the program;

The extent of the disease in any area into which expansion is planned;
The amount of money available;
The feasibility of expansion;
An appropriate balance between urban and rural population;
The political climate in the country.

The steps in planning the expansion are essentially the same as the steps in planning the first year of the program. Select the expansion areas, the priority diseases, and the target population. Determine the vaccine delivery strategy and the immunization schedule. Determine the resources required to implement the expansion.

Program Evaluation

After objectives have been established and program plans developed and implemented, evaluation becomes essential. Such evaluation will help answer three basic questions:

To what extent are the objectives of the program being achieved?
How did the program's plans, resources, methods, and operations contribute to achieved results?
How should the program modify its goals, objectives, plans, resources, methods, or operations in order to be more successful?

The ultimate objective of the program is reduction in disease morbidity and mortality. Section IV described how special and routine surveillance systems can be used to measure morbidity and mortality. As change in morbidity and mortality is the basic measure of program effectiveness, the priority need of adequate pre-program morbidity data cannot be underestimated.

Reductions in disease levels are achieved by effectively immunizing a susceptible population. The ability of the program to do this depends first on the quality of the vaccine and second on the success of inducing immunity in those given vaccines.

At what points along the "cold chain" should vaccine be sent for tests by supervisors or evaluators? One option might be upon receipt from the manufacturer. This is not necessary routinely if vaccine has been purchased from a manufacturer whose product is regularly tested by a certified testing laboratory, if a satisfactory flight schedule has been maintained, if conditions of storage during stopovers have been satisfactory, and if the vaccine was picked up promptly upon arrival and placed under refrigeration. If any of these conditions are doubtful, however, the vaccine should be tested.

Tests may also be conducted when vaccine has been to the field. When vaccine has been distributed from a central storage area to a provincial or district office, and then taken either to a health center or given to mobile teams and taken to an immunization site, samples should be tested. Supervisors can determine a schedule for selecting vials from different health centers/teams each month so that over a period of 1 year the more sensitive vaccines, such as polio and measles, used at each of the delivery points are evaluated at least once.

If the vaccine at these final points is satisfactory, then one is assured that conditions at intermediate points were also satisfactory. If the final points are not satisfactory, however, supervisors need to investigate back up the cold chain until all suspect sources of the problem are identified.

Another test point is shortly before the date of expiration. If a significant amount of vaccine will not be used before its date of expiration, then samples of the vaccine should be tested. Minimum amounts required to justify testing are as follows:

Measles--1,000 doses
Oral Polio--1,000 doses
Killed Polio--5,000 doses
BCG--10,000 doses
DPT--5,000 doses
DPT and Polio--10,000 doses
DT--5,000 doses
T--5,000 doses

If the amount of vaccine is less than those noted above, it is not worth the costs of the test and the vaccine should be discarded.

Whenever storage conditions have been doubtful the vaccine should be tested. When temperature indicators or available information suggest that vaccine may have been improperly stored at any point, the vaccine stored at that point should be tested. It is important to know when and where conditions have been unsatisfactory.

Immunity can be evaluated by conducting a serologic survey. While such surveys are useful, they are difficult for several reasons. Mothers and children are not enthusiastic about having blood samples taken. This could mean that following a survey fewer people will attend immunization clinics. Serologic tests are expensive and as it is often difficult to find laboratories with the capability to conduct serologic tests, such arrangements should always be made in advance. Thus, serologic surveys should be conducted infrequently. If immunization coverage objectives and objectives for the reduction of morbidity and mortality are achieved, the probability is high that vaccines are being protected.

There are two basic sampling techniques for serologic surveys: by cluster sampling and by simple random selection of individuals at the clinic site prior to immunization. The details of performing a serologic survey are beyond the scope of this manual and are available elsewhere. Table II lists all of the possible results from a survey using cluster sampling and gives possible interpretations for each result.

Even if a program is using potent vaccines which produce satisfactory seroconversion, it is still necessary to evaluate how successful any program has been in actually immunizing the target population. Following is a summary of the steps to be carried out in assessing typical rural areas using a cluster sampling technique. Slightly different procedures can be used in urban areas.

Selecting Villages to be Sampled. A list is prepared of all villages and their populations in the area to be evaluated. Cumulative population totals are compiled. In order to provide the necessary statistical reliability, it is necessary to have 30 sampling units examined from the total area. The total population for all villages is then divided by 30 to obtain the "sampling interval".

A random number between 1 and the "sampling interval" is selected. This number identifies the first village on the cumulative village population list to be included in the sample. The "sampling

Table II

POSSIBLE RESULTS AND INTERPRETATIONS FROM A CLUSTER SAMPLING SURVEY

Immunization Status after First Bloods	Results of First Bloods	Results of Second Bloods	Interpretations
(1) Immunized	-	-	Vaccine failure: Population did not convert following immunization.
(2) Immunized	-	+	Seroconversion due to immunizition or disease.
(3) Immunized	+	-	Laboratory or data collection error, or population may have had maternal antibodies at time of first blood.
(4) Immunized	+	+	Vaccine wastage: Population was already immune at time of immunization.
(5) Unimmunized	-	-	Normal: Susceptible population was not immunized and remained susceptible.
(6) Unimmunized	-	+	Susceptible population became immune from disease.
(7) Unimmunized	+	-	Laboratory or data collection error, or population may have had maternal antibodies at time of first blood.
(8) Unimmunized	+	+	Immune population remained immune.

interval" is then added to the random number selected. This number identifies the second village on the cumulative population list to be included. The remaining 28 villages are identified by continuing to add the "sampling interval" to the number selected previously.

Sampling Households and Children. In each village the initial household is selected randomly (e.g., by use of tax lists or house numbers, when available). In the initial households, the immunization status of each child in the age group to be evaluated is then recorded on a standardized form. Information regarding immunization status should be based upon immunization records where available.

The evaluator then proceeds to that household which is nearest the initial household, then to the household which is nearest the second household, and continues this process until seven children of the proper age group have been evaluated. The evaluator then proceeds to the next selected village and repeats the process described above.

When all selected villages have been evaluated, coverage can be determined. The most important measure of success is what proportion of individuals in the target group and area has been fully immunized with the antigen under consideration.

The evaluation previously described will provide valuable information on program results. It will not, however, tell specifically what types of changes are needed to achieve better results, since this evaluation does not identify the underlying problems which cause program deficiencies.

There are two basic ways in which underlying problems can be identified. First, program supervisors can determine problems they have encountered in performing their regular duties. Second, a formal periodic audit of program management and operations can be conducted by either program personnel, independent short-term consultants, or a combination.

Some of the questions which should be included are those pertaining to organizational location of the program. What is the overall organizational structure of the Ministry of Health? Are those units responsible for communicable disease control and immunization programs placed in such organizational positions that they can effectively carry out their responsibilities? If units in a number of different organizational locations have responsibilities as part of the immunization program, is there adequate coordination of planning, operations, and evaluation?

Other questions concern administrative structure and responsibilities of the program. To meaningfully answer the following questions, it may be useful to interview personnel in selected positions and observe their actual work performance.

What is the administrative structure of the program? Are sufficient resources provided to the immunization program to permit its operations to be carried out and its objectives to be met? Are responsibilities and relationships within the program clearly defined through the use of explicitly written task analyses and job descriptions ? Are the responsibilities are relationships recognized by staff members?

Do the task analyses and job descriptions accurately reflect employees' actual responsibilities and work performance? Are all of the tasks that must be performed to achieve objectives adequately covered by the combined responsibilities of program personnel? Are program personnel given adequate training? Is training consistent with the actual responsibilities of personnel? Are in-service training and retraining used, both routinely and when problems occur in performance?

Are personnel given adequate supervision? Do supervisors monitor performance? Are deficiencies in performance promptly noted and effective corrective methods taken? Is exemplary performance rewarded? Are salaries, work incentives, and opportunities for advancement comparable with those of personnel in other programs? Are salaries, work incentives, and opportunities for advancement seen by employees as being fair compensation for performance?

Are evaluations of coverage, immunity, and morbidity and mortality trends systematically carried out and used? Are adequate cost accounting records maintained? In determining overall program costs, are both capital expenditures (e.g., building, vehicles, refrigeration equipment, injectors) are recurring expenditures (e.g., personnel, vaccine, vehicle operation, maintenance and repair, needles and syringes, equipment spare parts) included?

Questions should also cover systems for procurement of material. What is the process used to place orders for material from suppliers (e.g., vaccines, injection equipment, vehicles, refrigerators and freezers, spare parts, etc.)? Is this process the result of an appropriate attempt to determine field needs? On what basis are suppliers chosen? Do contracts with suppliers specify that vaccines and other material must meet recognized international standards?

What is the monitoring process used between the time of ordering material and its arrival? What steps are taken in the event of unexpected delays? Are peripheral levels informed periodically of the status of their orders?

What procedures are used for customs clearance: Are such procedures routine and rapid? Are adequate holding facilities available and utilized upon arrival of material, particularly vaccines? What procedures are used for placing material in storage at the central warehouse once they have been cleared? Are entries in inventory records properly made? Are adequate storage facilities available and utilized?

Systems for maintenance and distribution of vaccines and material should be included. What system is used for maintenance and distribution at both the central and other levels? With regard to vaccines, does the system insure proper refrigeration not only in storage centers but also in transit from one point to another? Are refrigerators monitored, and is some system used to detect loss of refrigeration?

Is an adequate periodic maintenance schedule used for vehicles and other equipment? Is the distribution system based on documentation of need? Are proper security measures used? Are proper inventory records kept?

What system is used for reordering material? Is material ordered in sufficient amounts and in sufficient time so that program operations are not hampered by avoidable delays? What system is used for refrigerating vaccine at the field delivery level? Is the system adequate? Is it monitored?

Operations must be covered. What is the system used to inform and encourage the population to be immunized? Does this system make adequate use of traditional and civil authorities? Does the system utilize an effective variety of methods? Is there adequate coordination between personnel responsible for stimulating population participation and personnel responsible for immunizations?

Are program personnel given adequate training? Is the training consistent with the actual responsibilities of personnel? Are in-service training and retraining used both routinely and when problems occur in performance?

What procedures are used in setting up and operating immunization sessions? Is the assembly and movement of the population orderly and satisfactorily organized? Does the population have to wait an unnecessarily long time to be immunized? Is provision made for emergency repair or substitution of equipment? Is vaccine kept under correct refrigeration conditions when not in use?

Is an accurate means used for tallying the population immunized? Are immunization records properly filled out? Are immunizations limited to individuals of appropriate age and immunization history? Are sessions of sufficient length and frequency to give the population an opportunity to be immunized? Are mothers advised of possible vaccine reactions?

Are proper immunization techniques used? Are automatic injectors and needles and syringes adequately sterilized? Are proper dosages administered? Are partially used vials discarded at the end of the session? Are reconstituted freeze-dried ampules discarded at the end of the session?

Once a Program Audit has been completed, results and recommendations should be put in the form of a formal report. This report should then be used by program directors and supervisors as the basis for program modification. If reports are prepared on a periodic basis, it will be possible to document and observe program changes over time.

Immunization programs can play an important role by contributing to improved health in developing countries. Planning should be based on reliable data: specialized surveillance systems may need to be developed for the acquisition of useful information on immunizable diseases. WHO's Expanded Program on Immunization seeks to reduce morbidity and mortality from six target diseases, each of which has key issues yet to be resolved. Yet national priorities must be established with the epidemiological information available as well as attention to management feasibility, government commitment, and acceptability to the public. Program strategies and objectives should be designed for the first year of operation and modified with experience. Essential features of all immunization programs should be evaluation of changes in disease morbidity and mortality and comprehensiveness/completeness of coverage. Program audits identify underlying problems and help suggest necessary modifications for optimal program performance.

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LEPROSY

by

Robert M. Worth

Leprosy is a chronic infectious disease which in some cultures incurred an unwarranted social stigma. The stigma was predominantly related to the progressive and irreversible disfigurement associated with untreated leprosy. With the advent of modern chemotherapy, new cases of leprosy, when diagnosed early and placed under treatment, no longer pose any significant public health problem and usually present few personal or family problems.

Clinically, leprosy is characterized by lesions of the skin--infiltration, macules, plaques, papules, and nodules; by involvement and often palpable enlargement of peripheral nerves with consequent anesthesia, muscle weakness, and paralysis; and tropic changes in skin, muscle, and bone.

Two distinct major types occur: lepromatous and tuberculoid. Infections of an intermediate character are described as borderline (dimorphous), and an indeterminate form corresponds to earliest manifestations of the disease. In lepromatous leprosy diffuse skin lesions occur, as does invasion of mucous membranes of the upper respiratory tract along with the lymphoid system and some viscera; skin lesions may ulcerate; iritis and keratitis are common. The tuberculoid form is usually localized with discretely demarcated skin lesions, relatively early nerve involvement, and often, spontaneous healing in 1-3 years. Residual paralysis and anesthesia leading to trophic ulcers and other complications may result from either major form of leprosy if the disease is not diagnosed and placed under treatment early.

Almost any health aide or nurse can be taught to identify leprosy suspects accurately. Any primary physician or experienced physician surrogate can be taught to make the presumptive diagnosis by physical examination. The diagnosis cannot be considered final, however, without a confirming skin punch biopsy read by a pathologist or dermatologist experienced in leprosy work. If it is not feasible to obtain biopsies, the diagnosis can be confirmed by examining an incised skin smear; additional help in classification is elicited from lepromin test results. The lepromin test does not contribute to diagnosis and if a biopsy is taken, the lepromin test is not needed to distinguish the histological type.

Leprosy occurs chiefly in the tropics and subtropics. While prevalence rates of 5 per 1,000 or higher are found only in the tropics, socioeconomic conditions are probably more important than

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climate. The estimated world total is 11 million or more cases. A few countries with temperate climates have estimated prevalence rates of 1 per 1,000.

Leprosy is caused by Mycobacterium leprae. Although it has not yet been possible to fulfill all of Koch's postulates to "prove" the causative relationship, the bacillus is found in large numbers in all cases of lepromatous leprosy and in small numbers in most cases of tuberculoid leprosy. There is no basis for doubting that M. leprae is the etiologic agent.

Numerous studies indicate that the infection is transmitted from person to person by close contact. Bed contact evidently carries more risk than mere room contact. No insect vector has been proven, although the possibility exists.

Cohort studies of children and spouses of leprosy patients, followed through carefully repeated examinations over long periods of time, indicate that untreated lepromatous, "multibacillary" cases are the principal source of transmission to others. About 19% of the children and 5% of the spouses of such patients will later develop leprosy, though some variation in the risk is observed in different populations. Close contacts of untreated tuberculoid, "paucibacillary" cases, similarly followed, show no greater risk of leprosy than other members of that general population. Untreated lepromatous women do not transmit the infection to their unborn infants, but infants exposed after birth to an untreated lepromatous parent are at a 10%-40% risk and demonstrate peak disease incidence 6 to 9 years after first exposure.

The minority of exposed people who do develop the disease are probably distributed along the tuberculois-borderline-lepromatous continuum of clinical disease according to some genetic deficiency in cellular immunity, with the greatest deficiency occurring at the lepromatous end of the scale.

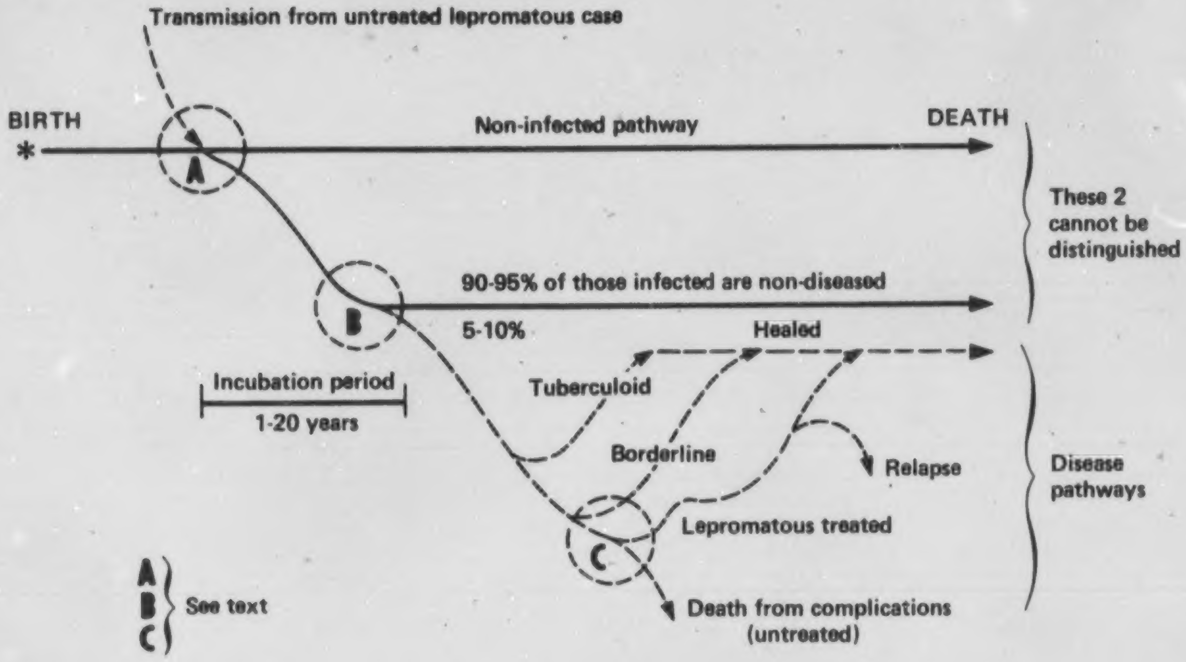
The top line on the accompanying illustration represents the usual and desired pathway through life: birth to death without infection by leprosy. At any point along that non-infected pathway, however, close contact with an untreated or inadequately treated lepromatous or borderline lepromatous case may lead to transmission (see A on the diagram).

The risk of transmission is predominantly controlled by environmental conditions which may lead to deviation from this pathway: the prevalence of untreated cases in that environment; the crowding that takes place within households; the social rules governing close contact in that place. Once infected, the risk of developing actual disease (see B on the diagram) is controlled by host variables governing resistance--90-95% usually have a subclinical infection and are "healthy".

General factors include age at exposure, nutritional status, physiologic stress (e.g. clinical breakdown during pregnancy is not unusual. Genetic factors include the immune response of the infected person, familial or racial selective forces.

The infectious period of the new lepromatous or borderline lepromatous, multibacillary case prior to the start of adequate treatment is indicated by C on the diagram. Treatment renders cases noninfectious rapidly but may not halt the signs and symptoms of disease promptly due to tissue reaction to dead or dying bacilli.

PATHWAYS OF LEPROSY


Transmission from untreated lepromatous case
BIRTH
*
Non-infected pathway
DEATH
A
These 2 cannot be distinguished
B
90-95% of those infected are non-diseased
5-10%
Healed
Incubation period
1-20 years
Tuberculoid
Borderline
Relapse
Disease pathways
C
Lepromatous treated
Death from complications (untreated)
A
B
C
See text

The long-range goal is to reduce the incidence of new cases of leprosy to zero by consistently breaking the transmission of the disease around every new or relapsed multibacillary case. This may be done through the methods discussed in this paper.

Methods of Estimating the Current Problem--Surveillance

Existing data may give some estimates of the incidence and/or prevalence of leprosy in the recent past in the population groups of interest. The gathering of data for the purpose of such estimates is often termed disease surveillance. Surveillance may be carried out in a "passive" or "active" fashion.

Passive surveillance implies that the central authorities who wish to gather the data are dependent on the diagnostic and reporting activities of some local authority. Passive methods are totally dependent on the coverage of the population by local clinicians and on their diagnostic accuracy and completeness in reporting and/or recording. Examples of passive surveillance follow.

Disease reports sent in to a central health authority by clinical facilities (out-patient clinic, hospital, quarantine office, home visitor, private physician, etc.). Such reports are notoriously incomplete (although usually required by local regulation). The clinician pays more attention to treatment than to reporting, which is often considered unimportant "paper work" harassment of a very busy person by some remote and unsympathetic official.

Periodic examination by the central authorities of existing local clinic or institutional records. Even though local hospital or clinic records are notoriously incomplete and/or illegible, they tend to be more complete than reports actually sent into a central health authority.

An illustration of the uses and limitations of the passive method may be found in Micronesia. In 1952 the South Pacific Commission provided a short-term leprosy consultant to help the leprosy surveillance activities in Micronesia, whose total population was about 60,000. The civilian authorities there had recently inherited from the previous military authorities a system of required leprosy reporting plus a central leprosy settlement for the required isolation and treatment of all lepromatous cases. When the consultant examined the existing records of the 90 patients in the leprosarium, he noted that a disproportionately large number of them had come from the small subdistrict of Pingelap, whose population consisted of only about 1,000 people. This examination of the records revealed a leprosy focus or "epidemic" which was later confirmed by active methods.

The patients in the leprosarium who had not come from Pingelap represented a small scattering from a wide range of sources in all of the other five districts. An examination of the leprosy case reports sent in from all six districts--though certainly incomplete--revealed the same pattern: low incidence rates (1/1,000/year) in five districts but a much higher rate in the Ponape district which included Pingelap atoll.

Active surveillance implies that the central authority carried out either periodic or special (one-time) direct surveys of the target population (or a sample of it) in order to estimate the incidence and/or prevalences rates of the disease under consideration. An incidence rate is here used as the number of new cases reported per unit of time, divided by the population at risk. A prevalence rate is the total number of cases found during a survey (or on an active case register) divided by the population examined (or at risk). This method requires the commitment of central resources but has the advantage of producing timely, more accurate and usually complete data in the form one wishes.

In the Micronesia example given above, the consultant (a highly qualified leprologist) visited the Pingelap atoll, examined about half the people in the one village there, and estimated an active leprosy case prevalence rate of about 5%. On his visit to the Ponape district health office, he discovered that the people from Pingelap were a highly in-bred group to which leprosy had first been introducted in 1918 by an immigrant case from the Gilbert Islands. The immigrant had become infected on Nauru, a "phosphate mine" island to which leprosy had been brought by people imported from southern China--a known leprosy focus--to work in the mines. This Pingelap "epidemic" was subsequently exported to two other villages in the district by outmigration of the Pingelap people due to population pressure. This three-village "epidemic" was clearly defined 13 years later by "active" survey of all three populations in preparation for an intensive control campaign to be described below.

One may ask, why the 13-year gap in Micronesia? The fact was that in 1953, the government faced a familiar set of problems: extremely limited health personnel and facilities; great difficulties in transport and communication; fully half the health budget consumed in evacuating critical cases to a remote and expensive secondary care hospital.

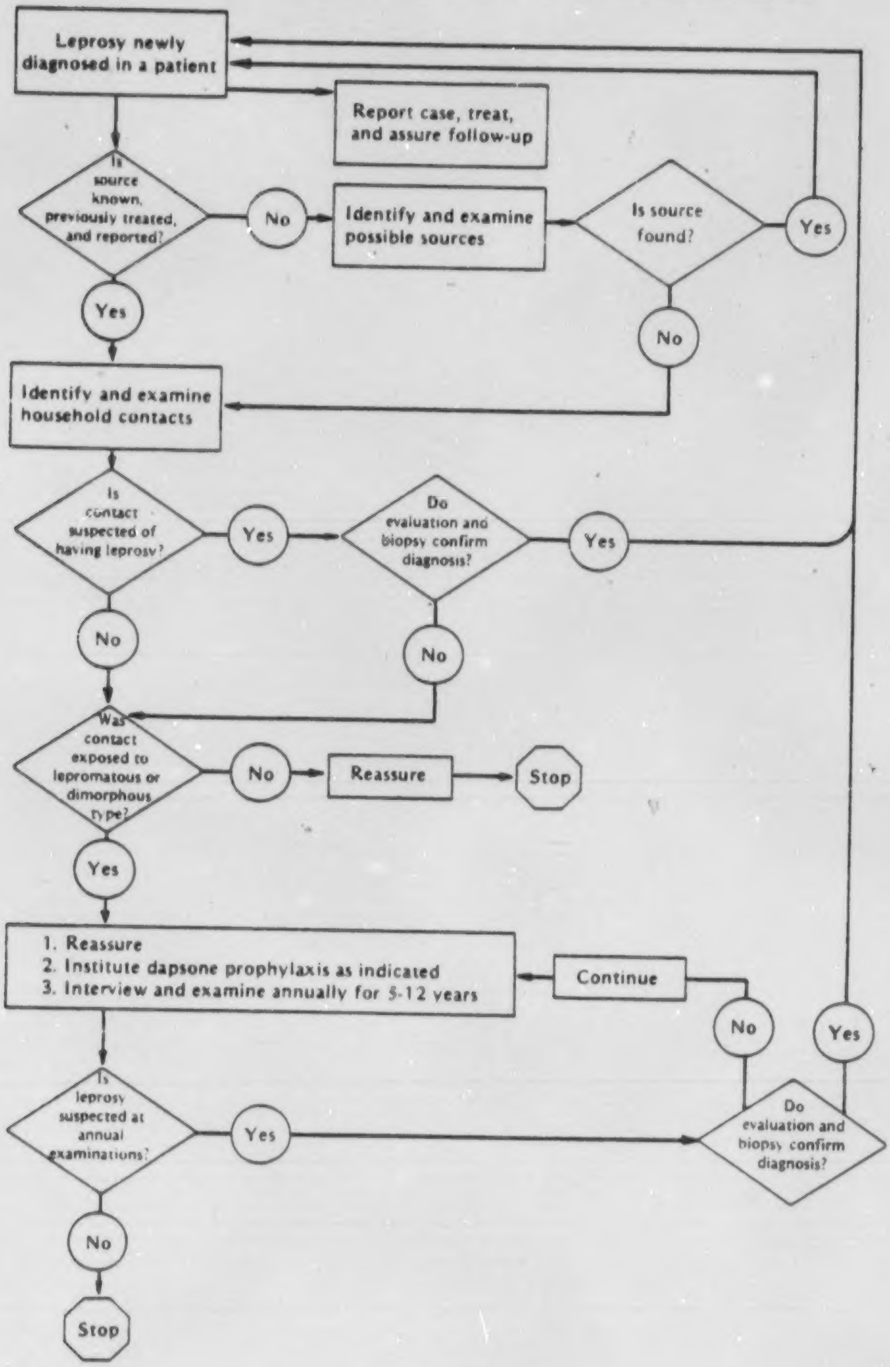
On the one hand was the fact that a majority of the population was not yet receiving even the bare minimum of preventive and primary health services; on the other hand was the fact that leprosy was a relatively minor problem except in one location. It was, therefore, decided that a very limited program would be undertaken. At that stage, a simple, common-sense approach was obvious. The infrastructure had to be built.

Evaluation of Existing Resources--The Infrastructure

The fundamental issue in any leprosy control program is whether to keep it separate or to integrate it into the primary care services for the population. The maintenance of leprosaria, with paid staff and an obligation for long-term full supoort of an increasingly institution-dependent population is an ever more costly road from which it is increasingly difficult to turn back. The patients, as well as the staff, become habituated to the institution.

As Figure 1 shows, the critical first element in control is the early identification and prompt, long-term treatment of lepeomatour, multibacillary cases. Sulphones apparently halt infectiveness of multibacillary cases within 2-3 months of the start of treatment, while rifampicin (unfortunately very costly) does so in a few days. Confinement to leprosaria does not contribute significantly to those objectives. In fact, it is probably counterproductive since the fear of confinement will often prevent a case from coming forward promptly for treatment. It is for these reasons that leprosaria are slowly vanishing.

Figure 1. Algorithm for Management of Household Contacts of Leprosy Patients


Leprosy newly diagnosed in a patient
Report case, treat, and assure follow-up
Is source known, previously treated, and reported?
No
Identify and examine possible sources
Is source found?
Yes
No
Yes
Identify and examine household contacts
Is contact suspected of having leprosy?
Yes
Do evaluation and biopsy confirm diagnosis?
Yes
No
No
Was contact exposed to lepromatous or dimorphous type?
No
Reassure
Stop
Yes
1. Reassure
2. Institute dapsone prophylaxis as indicated
3. Interview and examine annually for 5-12 years
Continue
No
Yes
Is leprosy suspected at annual examinations?
Yes
Do evaluation and biopsy confirm diagnosis?
No
Stop

Once an even rudimentary primary care system is in place, it can be successfully used for a basic integrated leprosy control program. One must first assure that each of the following questions can be answered in the affirmative:

Is there a health aide/post within one hour's travel (or available on monthly visits) of every village or urban district in which there may be a leprosy case? Is that aide trained and supervised in the identification of suspected leprosy (among other primary care duties)? Is the social situation such that every child, man, and woman is able to have his/her skin fully examined if necessary? Are the people bringing skin lesions to be inspected?

Is there an arrangement whereby a district medical officer is available to confirm suspected cases (via physical examination and skin smears read locally, and/or biopsy sent to a distant laboratory)? Are new case reports submitted to a central authority for every confirmed case? Do the district health officer, nurse/home visitor, health aide have a consistent and effective family education program for every new case: Does the health aide have a definite follow-up protocol for every household contact of a new case?

Is there an adequate and constant supply of DDS (Dapsone) and/or DADDS (Hansolar) plus B663 or rifampicin for resistant cases? Is the aide reliable and effective in carrying out the treatment protocol and documenting long-term drug treatment/ (Tuberculoid cases treated until inactive for three to five years, lepromatous cases for life.) Is there a district hospital where leprosy patients can go temporarily for treatment of complications and for family education? Is the staff there trained to handle such complications? Are the drugs available? Is periodic consultation (direct or via telephone) available from a national or regional leprosy expert?

Is there a national or regional leprosy expert who can assist in training; be available for consultation and reading biopsies; watch trends via passive surveillance of reports; monitor the program actively via periodic visits, sample surveys, record checks, and case reviews in every district; assure constant supply of and proper use of drugs?

If the answer is "yes" to each of the above, an integrated program exists. For every "no", a critical weak link in the chain has been identified. Extra effort should be focused on each weak spot until it is strengthened. When such a basic program is in place in any district, a move forward to one or both of the additional control activities described below can be made.

Planning Additional Control Efforts--The Suprastructure

During the past 15 years, research has identified two possible additional control methods beyond the early identification and treatment of every lepromatous case. Both are procedures which can be used to protect people exposed to the untreated lepromatous case, rather than just wait for disease to occur.

It is probable that a partial antigenic similarity exists between M. leprae and M. tuberculosis. Because of this, several carefully controlled trials of BDG have been carried out in high prevalence leprosy populations (Uganda, Papua-New Guinea, Burma) to test the vaccine's protective effect against leprosy. The enthusiasts have speculated that mass use of BCG in children for tuberculosis protection will also control leprosy. However, the controlled trials have not shown a consistent pattern. There is apparently a long-lasting, 60% reduction in leprosy incidence related to BCG in Uganda; a much lower protection (which does not appear until after five years) in New Guinea; and virtually no protection in Burma. Apparently then, mass BCG will not be the "magic bullet" and will not replace the basic diagnosis and treatment program outlined above. It may be of supplemental value, however, if used consistently for affected families and in all very young children in villages where lepromatous cases appear. Work is continuing to try to develop a more consistently effective immunization method.

Although children born into the family of a lepromatous leprosy patient after the case has started treatment have no extra risk of subsequent leprosy, others in that family (older siblings, adults) were exposed and they run a 5% to 10% risk of leprosy. It has been demonstrated that the administration of DDS by mouth (in India) or DADDS by injection every 2½ months (in Micronesia) for 3 years during the incubation period in such exposed people will sharply reduce their subsequent incidence of leprosy. Consistent maintenance of long-term oral medication in both difficult and administratively expensive.

The 10-year follow-up experience in Micronesia has shown that: DADDS is safe and efficient to administer without, as yet, any unusual emergence of sulfone-resistance. Not everyone will cooperate but families of patients are more likely to do so. If lepromatous cases are not simultaneously and continuously kept under good treatment, they will infect or reinfect people as soon as the preventive treatment is stopped and, thus, re-establish the chain of infection.

This experience has shown that preventive treatment is supplemental to and dependent upon a good basic case identification and conscientious treatment program. It is not a substitute. An immunization program may have a protective effect for years after it is administered but this "incubation period" preventive treatment (analogous to giving INH to someone who has recently undergone a conversion of his/her tuberculin test) leaves the person susceptible to re-exposure as soon as the drug is stopped.

It is clear, then, that the "maximum" program with our current knowledge and tools would be to build and maintain a good integrated case identification and treatment program (as outlined above) in every locality where leprosy occurs. When that program is functioning, take two additional steps to break transmission, but do not do it in any way that will degrade the basic program (dilution of resources, etc.). Both of these steps involve an injection procedure that is quite acceptable in most countries.

If BCG is used, make sure that it gets to every young child in leprosy-affected villages. If BCG is not used (due to decisions made in the tuberculosis program), try to get it into every young child in families with lepromatous leprosy. Also, supply the health aide with, teach him/her how to, and supervise the routine administration of 1.5 cc (1.0 cc for ages 6 months to 2 years) DADDS IM every 2½ months for 3 years (15 injections) to every household or close contact of every new lepromatous or borderline lepromatous case. When this program first starts, it would be better (if feasible) to include household contacts of all lepromatous or borderline lepromatous cases first placed under treatment during the past 5 years, since most of these contacts would be still "incubating" the infection.

The additional resources needed to carry out these two additional steps are minimal if the infrastructure is present. BCG is inexpensive, need be given only once, and can easily be given by a health aide. DADDS is also inexpensive and can be given by a health aide, who needs to visit each eligible family only 5 times per year for 3 years. On this basis, and armed with the expected number of new lepromatous cases in each district, plus the estimated average birth rate and household size in that district, one can make fairly accurate estimates of the number of injections needed to be given per health aide per month. For example, assume a health post serving 1,000 people, whose birth rate is about 30/1,000/year, the average household size is 6, and the expected number of new lepromatous or borderline lepromatous cases is 1/1,000/year (based on the actual experience of the last 5 years).

Such a "maximum" program can be expected to considerably shorten the time required to bring leprosy under control in a high prevalence area. For the sake of discussion, one might assume the following starting circumstances:

New cases/1,000 population/year = 1 lepromatous or borderline (20-year duration of Rx)
+
2 tuberculoid (5-year duration of Rx)
3/1,000/year

Prevalence of treated cases = 30 cases under treatment/1,000 population.
(150 DADDS injections/1,000/year
+105 preventive injections/year)

The protocol-required household contact examinations are assumed to be part of the basic program.

After		Basic Program*	Maximum Program**
5 years	Incidence	2,5/1,000/year	1/1,000/year
	Treated case prevalence	25/1,000	20/1,000
10 years	Incidence	2/1,000	0.4/1,000
	Treated case prevalence	20/1,000 (100 DADDS treatment injections/year)	12/1,000 (60 DADDS treatment injections/year+60 preventive)
15 years	Incidence	1.5/1,000/year	0.1/1,000/year
	Treated case prevalence	15/1,000 (75 DADDS treatment injections/year)	6/1,000 (30 DADDS treatment injections/year+30 preventive)

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* Based on analogies to well-run basic programs. (Average 3%-5% fall in incidence/year, treatment only).

** Based on analogies to experience in Pingelap program (where BCG was not used) and assuming a well-run basic program plus preventive treatment (67% fall in 1st 5 years, slower thereafter).

If these assumptions are true, the extra workload of 8-9 shots per month for the health aide would, at the end of 15 years, have reduced the incidence of new cases (and hence of disability and hospitalization due to complications) to 1/15 of what it would otherwise have been with the basic program alone. The aide's case workload (prevalence of treated cases) would be down to about 1/2 (a slower fall due to the old lepromatous cases requiring continued treatment) and his/her preventive workload would be down to about 1/3 of what it was at the beginning.

The four pieces of data necessary to determine if the program is on schedule toward meeting such a set of specific goals can be generated by the program itself.

New case reports/year/subdistrict population estimate x 1,000.

Number of cases currently under treatment/subdistrict population estimate x 1,000.

Number of DADDS preventive shots/year/number new lepromatour or borderline lepromatous cases/year.

Number household contact examinations per year per lepromatous or borderline lepromatous cases per year.

If the average household size is 6 (5 contacts), there should be an average of 15 DADDS preventive shots being given per year and documented on a contact roster for each such new case. (5 for this year's new cases, 5 for last year's, and 5 for the year before that).

If the average household size is 6 (5 contacts), and if they are examined annually for 10 years after the start of treatment of the lepromatous or borderline lepromatous case, and if such cases are under treatment an average of 20 years, then for every such case under current treatment, there should be an average of 2½ annual contact examinations being done and being documented on an examination roster.

The accuracy of the raw data being sent in by or recorded locally in a subdistrict can be assessed periodically by a national or regional staff person visiting for that purpose, preferably on an unannounced, sampling basis.

Potential Problems

In order to develop and run the program outlined above in any country or region, two potential problems must be faced--the need for special personnel and special supplies.

The key to success is the identification, training, and retention of one dedicated and enthusiastic, indigenous leprosy physician. There are leprosy training centers where any indigenous physician can acquire all the specialized knowledge necessary in 6-12 months of training. Leprosy work is not popular, however. It is generally not regarded as glamorous and affords no opportunity for a lucrative private practice on the side. If, however, one can identify an enthusiastic and able person willing to dedicate himself or herself for a long term to leprosy work, the greatest problem has been solved. After specialized short-term training at an appropriate regional center, such a person, if given proper administrative support and opportunity to get occasional consultation, can go about the task of training, inspiring, and monitoring the effectiveness of leprosy work done in the "infrastructure" described above. A key element needed in the character of such a regional or national leprosy leader is patient, persistent, conscientious attention to detail.

Arrangements must be made for forwarding skin biopsies in formalin to a pathologist or dermatologist qualified to confirm leprosy diagnoses. This is a skill that can be acquired in a few weeks at any of several leprosy training centers. Voluntary leprosy agencies may be able to provide this service in some localities.

Special arrangements must also be made for a constant supply and proper use of the drugs mentioned earlier. DADDS should not be used initially as the primary treatment for a leprosy patient unless one can assure constant, regular dosage for the required period. Otherwise there is too great a risk of developing sulfone-resistant strains of M. leprae. Since in about 18% of multibacillary patients the use of DADDS alone will not be sufficient treatment, combined therapy with another, non-sulfone drug should be considered. B663 is less expensive but must be used for long periods of time and is sometimes not popular due to skin pigmentation changes. Rifampicin needs to be used at only 600 mgm per day for 90 days, but is very expensive and may have untoward side-effects, especially if therapy is interrupted. If resources are sufficient, all multibacillary cases should be given a 90-day rifampicin course along with long-term DADDS. This combination should result in virtually all multibacillary cases reaching an inactive status in about 7-10 years.

If this treatment regimen for all multibacillary cases is too costly, an alternative is to start all such cases on DADDS alone, treat carefully and persistently for 6-12 months, then give a 90-day course of rifampicin in addition to the DADDS to those few patients who are not (or no longer) progressing satisfactorily on DADDS alone. Multibacillary cases must be kept under treatment and observation for very long periods of time, since late reactivation (with or without sulfone resistance) is not uncommon.

Leprosy has actually vanished from populations where its prevalence formerly was high--even in rural areas. Israel has not had an indigenous secondary case in 30 years. There are several subdistricts of rural Hawaiian populations where there has not been a new indigenous case for 20 years. The incidence of new leprosy cases in Japan is very close to zero. It requires patient, conscientious, persistent work; but it can be done, even by use of the "basic" methods alone, without the new preventive techniques for speeding the process.

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TUBERCULOSIS

BY

Laurence S. Farer

Tuberculosis is a communicable, bacterial disease which results from infection with tubercle bacilli. Although once considered a chronic, relapsing disease, today tuberculosis is treatable, curable, and preventable. Tuberculosis can be traced back to mankind's early history: it has been recognized for centuries, but its protean nature led to its being considered many supposedly separate diseases called by a variety of names. An understanding of tuberculosis in modern terms came with the scientific development of anatomy, pathology, bacteriology, and clinical diagnosis which culminated in Koch's discovery of the tubercle bacillus in 1882. Although the communicability of the disease had been known long before Koch, the progress in microbiology that followed his discovery provided the scientific basis for the current view of tuberculosis as a systemic infectious process with varying clinical manifestations.

Tuberculosis is worldwide in distribution and strikes the rich and the poor, all ages, all races, and both sexes. Improvements in diet, housing and living conditions in modern times--where they have occurred--have contributed to a decline in tuberculosis mortality and an accompanying decline in new cases. The advent of chemotherapy three decades ago accelerated these trends. Declining tuberculosis death and case rates are now apparent throughout the world. Nevertheless, tuberculosis still ranks among the major health problems in the world, especially in the developing countries. As the incidence of the disease decreases, cases become increasingly clustered in identifiable segments of the population, especially those who live to an inordinate degree under conditions of poverty, ignorance, and social privation. The aged, particularly in urban communities, and those generally classed as members of low socioeconomic groups have more tuberculosis than is found in the rest of the population.

The World Health Organization (WHO) estimates that more than half a million people die from tuberculosis annually. Despite the remarkable decline in mortality, tuberculosis remains in many parts of the world--mainly in the Western Pacific, the southern part of Africa, and South America--among the leading causes of death. Even in many technically advanced countries where it is considered uncommon, tuberculosis often causes more deaths than all other notifiable (communicable) diseases combined.

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It is estimated that there are approximately 7 million cases of infectious tuberculosis in the world, more than three quarters of them in the developing countries. About 3½ million new infectious cases occur annually. In some areas of Africa, Asia, and Oceania the reported annual incidence of pulmonary tuberculosis is 200-500 cases per 100,000 inhabitants.

In developing countries, the annual incidence of new tuberculous infections is over 2% of the total population, In countries with low tuberculosis prevalence, the annual infection rate is decreasing by about 10% per year; whereas the fall is much slower in high prevalence countries--some of which the infection rate has remained constant for the last decade.

Tuberculosis is caused by mycobacteriacalled tubercle bacilli: the species which infect man are M. tuberculosis, M. bovis, and M. africanum. Other mycobacteria, of which there are many, are not tubercle bacilli and disease caused by mycobacteria other than tubercle bacilli is not tuberculosis.

M. tuberculosis is an obligate parasite. It infects humans, other primates, and other animals associated with man. M. bovis causes tuberculosis in cattle, related species, and other animals associated with cattle, including man. It differs from M. tuberculosis in a number of ways which can be detected in the laboratory. M. africanum has characteristics intermediate between M. tuberculosis and M. bovis. The different tubercle bacilli cause histopathologically and clinically indistinguishable disease in humans.

Mycobacterial cells, when stained, strongly retain the dye which is not removed by acid-alcohol solutions. This property is known as acid-fastness. Identification of acid-fast bacilli by microscopic examination of properly stained specimens is of the utmost diagnostic and epidemiologic importance in tuberculosis control programs.

Tuberculous infection in humans is generally acquired by inhalation of droplet nuclei which contain tubercle bacilli. Persons with pulmonary tuberculosis expel aerosols which contain these droplet nuclei into the air when coughing, sneezing, talking, or singing. Droplet nuclei are so small (1-10 mm in diameter) that air currents normally present in the environment keep them airborne. Once released from an infected individual, they may become dispersed throughout the environment and can be inhaled by a susceptible host. Infected persons also shed larger particles laden with tubercle bacilli; but when large particles are inhaled, they impact on the walls of the upper airways where they are trapped in the mucous blanket, carried to the oropharynx, and swallowed or expectorated.

The droplet nuclei when inhaled are able to bypass the normal protective barriers afforded by nasal hairs and the mucociliary escalator of the bronchial tree. These tiny particles can reach the most peripheral portion of the bronchial tree and lodge in the alveoli where they can establish a focus of infection. The longer the period of exposure to the contaminated environment and the greater the concentration of tubercle bacilli in the air, the greater the likelihood that infection will occur.

Tuberculosis is not a highly infectious disease. Fairly prolonged or frequent association with an infectious source is generally required for infection to be transmitted. For this reason, the greatest hazard of infection is borne by persons who share the same environment with an infectious, usually unsuspected, case of tuberculosis. The size of the bacterial population in the source case, the efficiency with which the bacilli are being excreted, the presence of absence of good ventilation in the environment in which exposure takes place, and the susceptibility of the person who is inhaling the infectious particles all play a role in determining whether or not infection will occur.

Although the airborne route is the main route of transmission, it is possible for tuberculous infection to be transmitted via the gastrointestinal route or by direct inoculation through the skin or mucous membranes. The gastrointestinal tract is not a common portal of entry for M. tuberculosis. For M. bovis, the gastrointestinal tract is probably the chief portal of entry in humans; it is a health hazard primarily for children who become infected by drinking milk contaminated with tubercule bacilli.

Milk pasteurization and slaughter of infected cattle have made bovine tuberculosis an uncommon disease in many parts of the world, but where these measures have not been employed, M. bovis may still be a significant source of infection. Direct inoculation is a very unlikely way to acquire tuberculous infection but may be an occupational hazard for laboratory workers, pathologists, surgeons, and other medical and paramedical personnel in whom a break in the skin or mucous membranes may permit penetration of bacilli.

Because transmission is chiefly by the airborne route, it is possible to reduce the likelihood of infection by preventing an infectious aerosol from entering the air or by effectively removing the infectious particles from the air once they are present. Effective chemotherapy keeps tubercle bacilli out of the air by reducing the number of organisms in the sputum as well as the frequency of coughing. Covering the nose and mouth while coughing or sneezing reduces the number of droplet nuclei which become airborne. Once in the air, infectious particles can be removed by ventilation with fresh air, preferably exhausted to the outside where tubercle bacilli which are exposed to sunlight will be killed by ultraviolet irradiation.

If a tubercle bacillus successfully reaches the lung of a susceptible host, the result may be a localized focus of infection. The initial response to the deposition of this foreign particle is a nonspecific, inflammatory reaction which, because of the normal ventilatory pattern, usually occurs in the peripheral portion of the lower lung. The infection spreads to other parts of the body, including other portions of the lungs. During this time the host's specific immunologic response begins to operate. The response, which develops over a period of several weeks, usually proves adequate to limit further multiplication and spread of bacilli. The inflammatory process generally subsides, leading to healing. By this time the tuberculin reaction has become positive, and a skin test will indicate that the person is infected.

In a very small percentage of infected persons, the progress of the infection outpaces the host response, and progressive disease occurs. The progression may be local at the site of the original implantation; or it may be at some distant location where bacilli have spread; or there may be generalized progression at all the sites in the body where bacteria have been deposited (miliary tuberculosis). In the vast majority of cases, however, the initial infection heals spontaneously and its presence is probably not known to the host. If there are signs and symptoms of illness during this initial infection, they must be rather nonspecific and mild as it is unusual for persons at this stage to seek medical attention.

Once the initial infectious process subsides, it can take a variable course. In most infected people, healing is permanent. In a small percentage of those whose initial infection heals, the infectious process will undergo a recrudescence at a later time in their lives, and they will develop those overt clinical manifestations recognized as tuberculosis. Illness may develop after an interval of years or decades when tubercle bacilli that have persisted in the body begin to replicate and produce disease. Although foci anywhere in the body may be the sites of late progression, the lung, especially its upper portions, is the most common site. Pulmonary tuberculosis is epidemiologically significant because of its potential for airborne transmission of infection.

Tuberculous infection provides relative immunity against tubercle bacilli which may subsequently be inhaled. This immunity is not absolute as evidenced by the fact that tuberculosis can occur in persons in whom immunity has been artificailly induced through immunization. Nevertheless, most tuberculosis is probably not the result of a recent reinfection but of a flare-up of the remote initial infection. It is not known why foci of viable bacilli persist in some persons, nor why these dormant foci later become the source of progressive disease. The ability of the host to keep the dormant infection under control may be diminished by factors, such as age, concomitant diseases, hormonal changes, and malnutrition.

Tuberculosis may simulate or occur concurrently with almost any disease. Although tuberculosis usually comes to medical attention because of symptoms, many patients, even some with extensive disease, have insidious onsets. Some patients are truly asymptomatic. Although it usually affects the lungs, tuberculosis can occur in almost any part of the body and may show up in unusual ways. Once the disease is considered, the diagnosis of tuberculosis is straightforward, but unusual manifestations may challenge the best diagnostic skills of the physician.

In contrast to the risk of initial infection which is more closely related to environmental than to host factors, the risk of developing disease once infected appears to be more closely related to host factors than to environmental factors. Many conditions are known or thought to affect the immunologic competency of the host. Among these are other diseases, prolonged fatigue, malnutrition, emotional disturbance, stress, and alcoholism.

Before tuberculosis can be diagnosed, it must be suspected--often on the basis of signs and symptoms. A suspicion of tuberculosis should serve to initiate collection of further data on which to make a differential diagnosis in a reasonable period of time. Patients can be characterized as having generalized or systemic signs and symptoms, pulmonary signs and symptoms, signs and symptoms related to other organs, or a combination of these. Extrapulmonary disease may occur with or without accompanying pulmonary tuberculosis. Patients usually seek medical attention because of symptoms, such as coughing, loss of weight, and fever. Medical care providers must, therefore, be able to diagnose cases of tuberculosis and to be on the look-out for them.

Chest roentgenography (X-ray) can demonstrate the presence, location, extent, and characteristics of pulmonary disease. However, the diagnosis cannot be established on the basis of roentgenologic findings alone although the character and location of infiltrates may suggest tuberculosis. Tuberculosis may produce almost any form of pulmonary abnormality roentgenographically and similar abnormalities may occur in any number of other pulmonary diseases.

A suspected diagnosis of tuberculosis can be confirmed only by bacteriologic tests. Since not all acid-fast organisms are tubercle bacilli, culture identification is mandatory for proper diagnosis and therapy. However, the simplest and most direct way of determining the infectious organism is microscopic examination of sputum. The examination can be performed readily by trained auxiliary staff. It takes a very short time and gives an indication of the number of organisms being excreted, and thus the patient's infectivity. Although every effort should be made to obtain bacteriologic confirmation of a suspected diagnosis of tuberculosis, a negative bacteriologic result does not rule out the diagnosis. Sometimes it is necessary to rely on a presumptive clinical diagnosis. Whether or not to treat such presumptive cases depends on local resources and priorities since they are not likely to be infectious and are of less importance from a public health point of view.

Assessment of Existing Situation

In order to establish clear priorities for national tuberculosis programs, it is necessary to understand and consider the dynamics and interactions of epidemiological factors as well as the impact of tuberculosis control measures in any given area. Sound spidemiological and operational information are essential.

Collected data can be used to measure the problem at a point in time; to compare the situation with past and future points in time; to compare the situation in one area with that in other comparable areas; and to develop predictive models. Of greater practical importance, data can be used for program planning and modification so that something can be done about the problem. Information is needed to set priorities, allocate resources, and evaluate progress in achieving program objectives.

The usual epidemiological indicators are mortality, morbidity, and infection. They can be examined in terms of prevalence and incidence, and as both numbers and rates: the various indices impart different information. For instance, prevalence of infection in a population reflects its cumulative, historical experience with the tubercle bacillus but does not explain the current situation. Incidence of infection reflects current or recent transmission of infection. Both give an indication of the magnitude of the tuberculosis problem in a community. Similarly, the number of new cases may be important for organizing services, but the case rate is more useful for comparing the relative seriousness of the situation in different places or at different times, especially if the population base varies. Variations between population subgroups must also be considered; tuberculosis is not uniformly distributed in countries or communities. The problem must be assessed on terms of age, race, socioeconomic, and geographic distribution.

Mortality data may be incorrect and incomplete, especially in developing countries. Furthermore, since the introduction of effective chemotherapy, mortality data have largely lost their value as an index of the magnitude of the tuberculosis problem. However, in a crude sense, a high mortality rate is a clear indication of an inadequate program.

Morbidity data could provide a measure of the tuberculosis problem; but, unfortunately, routinely collected data are incomplete and unreliable. Notification data on the incidence are inaccurate and so may underestimate or overestimate actual rates. Such data may reflect the intensity of case finding efforts rather than actual epidemiological trends. They are particularly deficient in bacteriological information and may depend on vaguely defined, uncertain clinical criteria for diagnosis.

Surveys have been made to measure the tuberculosis problem in those developing countries for which reliable mortality and morbidity data are generally unavailable. Prevalence surveys are a formidable undertaking but can give a fair estimate of the problem with good sample selection and efficient execution. Information can be obtained on the relative significance of epidemiological indices, such as excretion of tubercle bacilli, symptoms, chest radiograph abnormalities, and positive tuberculin skin tests. By repeating surveys at intervals, incidence estimates can be made, the fate of patients can be determined, and changes in the situation can be recognized. However, it has generally not been possible to undertake such surveys frequently enough to follow trends. Longitudinal surveys, such as one consisting of long-term follow-up of a population in India, can clarify the epidemioloigical dynamics of tuberculosis and determine those population groups that would derive the greatest benefit from specific control measures. A survey of this type provides information on the flow of individuals from one status to another (e.g., from uninfected to infected to diseased to cured) and on indices, such as spontaneous healing, relapse rates, and case-fatality rates. Longitudinal surveys permit prediction, based on probabilities derived from the data, and can be used for the construction of predictive models. Unfortunately, surveys are expensive and difficult to carry out.

Currently, the two epidemiological indices most relevant to measurement of the tuberculosis problem in the community and to program strategy are (1) the prevalence of tuberculosis patients excreting bacilli demonstrable by direct smear examination and (2) the age-specific prevalance of tuberculous infection as demonstrated by tuberculin testing.

A comprehensive survey to determine the prevalence of tubercle bacilli excretors should yield reliable information on the magnitude of the pool of infectious individuals in the community, but it is difficult to accomplish. Such surveys require considerable resources and technical skill. Furthermore, owing to the relatively low frequency of smear-positive tuberculosis, such a survey requires a large study population. Nevertheless, the prevalence of tuberculosis patients whose sputum contains tubercle bacilli demonstrable by direct smear microscopy is the most informative, crucial index for quantifying the tuberculosis problem and for following its trend. Untreated patients whose sputum is positive by direct microscopy are highly infectious and are the ones primarily responsible for transmission of infection in the community.

It is much easier to measure the age-specific prevalence of infection, especially in children, and to estimate its trend that to measure the prevalence of excretors of tubercle bacilli. Measurement of infection rates can be undertaken in much smaller study populations. Tuberculin surveys of a representative sample of unimmunized children at a specified age (e.g., at school entrance age) can be carried out without difficulty in most countries. However, their design and statistical interpretation become more complicated in countries where a substantial part of the age group under investigation has received BCT vaccine (which produces a positive tuberculin skin test reaction) and in areas with a high prevalence of nonspecific cross-reactions (produced by non-tuberculous mycobacteria). The annual incidence or annual risk of infection for the surveyed population can be derived mathematically from age-specific prevalence data from a single tuberculin survey, or preferably, from at least two tuberculin surveys at different times in the same population. It should be appreciated that where there is a large reservoir of infected persons, there can continue to be a substantial case load and a high annual incidence of new infectious cases in the older age groups even though there may be very little transmission of infection to children and young adults.

In order to prepare a national tuberculosis control program, basic data must be collected on:

the epidemiology of tuberculosis;
demography (including ethnic and other important groups and their behavior patterns with regard to health and illness);
communications and transportation;
administrative structure;
community and health development programs;
the structure of the health services and their coverage of the population; and
the availability of professional, auxiliary, and voluntary manpower, and other resources at all levels.

Among questions to be asked are the following: Is the tuberculosis control program centrally planned and programmed for the whole country in a coordinated manner? Is the program countrywide or concentrated in the urban areas? Is there a permanent organizational framework for tuberculosis control or are there episodic "campaigns"? Is the program run as a specialized service or is it integrated at the peripheral level into the basic health services?

Do basic health services exist at all levels, and are they able to cope with the provision of services for tuberculosis? Have simple, standardized techniques and procedures for diagnosis, treatment, and prevention been described in manuals and work instructions which are understandable to workers at all levels? Has training been provided or can it be provided to workers at all levels in order that they can carry out the work?

Does laboratory support exist? Are drugs available at all levels and is there a system for their distribution from the central level to the peripheral level to the patient? How is the tuberculosis program financed? What role do voluntary agencies, such as

Tuberculosis Associations and missionary medical organizations, play in supporting the program and in providing services? Are resources being maldistributed or misused as, for example, in providing hospital-based care (which has been shown to be expensive and irrelevant for treatment success) or in performing mass radiography (which has been shown to be expensive and inefficient as a case-finding method)?

These types of questions must be asked in order to determine what components of the existing program need to be modified or eliminated and what missing components need to be added. This information is then organized into a schedule for the development of preventive and curative anti-tuberculosis activities within the basic health services aiming at covering the whole population within a reasonable period of time. Based on this schedule, the program should specify the approach to be followed, the resources to be allocated, the staff to be trained, and the operational objectives.

Planning a Control Program

Control of tuberculosis is influenced by disparate epidemiologic, social, economic and political factors. The prospect for continuing reduction of tuberculosis incidence is a realistic concept in countries which have organized modern health facilities and adequate fiscal support. Effective methods are available for controlling the disease and have been applied successfully for several decades. The major gains have been in children; for adults, especially those in the older age groups, the decline in case rates has been disappointingly slow. The annual case load in the older age groups will remain considerable for many years to come. Eradication of the disease in any part of the world by the end of the twentieth century is unlikely.

Principles for the control of tuberculosis do not change from country to country, whatever their stage of development. How the principles are applied will vary since they must be adapted to local circumstances. In order to have a real impact on the control of tuberculosis in the very large number of countries where it remains a serious public health problem, it is especially necessary to make the best possible use of limited resources.

Since diagnostic, preventive, and curative method can be both simple and inexpensive, the control of tuberculosis can be given a high priority without depleting the entire health budget. An effective national tuberculosis program can be delivered in almost any situation provided that planning and application are guided by a clear understanding of the epidemiological, technical, operational, logistic, economic, and social aspects.

The place of tuberculosis control in a country's overall health policy must be recognized so that it can be related to other needs. Among these are the strengthening of basic health services, expanded immunization programs, and control of other diseases, such as malaria and leprosy, which are prevalent in developing countries. Tuberculosis services cannot absorb a disproportionate share of the limited trained manpower and financial resources of developing countries.

The organization of a national tuberculosis control program requires adequate planning, policy formulation, programming, implementation, monitoring, and evaluation. The emphasis given to either the curative or the preventive program component depends largely on the epidemiological situation and the resources available, but both components should be applied to some degree in almost all situations. Implementation of the program at the peripheral level (the actual delivery of services) should be supported by managerial teams responsible for supervision and evaluation of the peripheral and referral services and for in-service training. Evaluation must be an integral component of the program built in right from the beginning. Training should be program oriented and directed at all categories of health workers engaged in tuberculosis control. Overall coordination and direction must exist at the central level.

For a national tuberculosis program to be effective, it must be countrywide; it must be permanent; it must be adapted to the expressed needs and demands of the population; and it must be integrated into the community health structure. The program cannot succeed if it is localized in the cities and large towns and is out of reach of the bulk of infected individuals who may be found predominantly in rural areas. The program cannot be episodic because transmission of tubercle bacilli within a community is continuous, and new cases of tuberculosis will develop for years to come. The program must be conceived and organized for the convenience of the consumer rather than for those who provide services.

Integration of the program into the community health structure is possible because of the simplification and standardization of techniques and procedures. The necessary skills to achieve the objectives of a national program are within the capacity of any medical doctor and most medical auxiliaries who will have to deliver program services in the field and make it succeed.

A national program needs to be modern; it must make rational use of the available methods which are effective, simple, and cheap. Some national programs, based on hospital or sanatorium treatment, are not modern; other programs, considered modern because they include expensive drugs and sophisticated diagnostic equipment, are not national since they do not meet the needs of the whole country; some programs are neither modern nor national. The successful program will have to obtain acceptance of new approaches to tuberculosis control. In some areas, there is still insufficient dissemination of scientific knowledge on which current, simplified technologies and program policies are based. There is still widespread reluctance among the medical profession to use unsophisticated procedures which, to a large extent, can be delegated to non-specialists and even to non-medical health personnel. In many developing countries, the health infrastructure is still too weak to provide comprehensive health care, especially in rural communities. The key to overcoming these obstacles lies in the training of staff, the organization of services, and continuous program evaluation which leads to correction of performance deficiencies.

The ultimate purpose of a national tuberculosis program is the reduction of human suffering and the eventual elimination of death, disability, emotional trauma, family disruption, and social stigma due to tuberculosis. The focus of the attack must be on the tubercle bacillus. Evidence indicates that the natural balance is against the survival of the tubercle bacillus. The conditions which limit its propagation are:

(1) it must cause a lesion which breaks through to the surface to escape from its host;

(2) it succeeds in producing such lesions in only a limited proportion of infected persons.

The expectation that tuberculosis will eventually be eradicated is reasonable and justifies shaping a control program toward that end. For the eventual eradication of tuberculosis, it is necessary only that transmission be held permanently below the level at which a given number of infectious cases succeed in infecting an equivalent number to carry on the succession. If in successive periods the number of infectious hosts is continuously reduced over a sufficiently long time, the end result must be the extermination of the tubercle bacillus. These basic principles were stated over 40 years ago, before the advent of chemotherapy, by the epidemiologist Wade Hampton Frost. Even then he advised that control programs be focused on the "open" cases.

Thus, the immediate object of tuberculosis control is to break the chain of transmission of infection. This can be achieved by detecting, as early as possible, the sources of infection in the community (usually persons whose sputum is so heavily positive that tubercle bacilli can be detected by direct sputum smear microscopy) and rendering them noninfectious by chemotherapy. If this could be accomplised with maximum effectiveness and efficiency, there would be little need for BCG baccine, a preventive measure directed at persons who are not yet infected. However, where case finding and treatment are still inadequate to cope with the volume of infectious cases as in most developing countries, and where the risk of becoming infected is high, the use of BCG vaccine, particularly in the young, is considered necessary.

In technically advanced countries with low tuberculosis provalence and little transmission, BCG protection for the uninfected is less relevant. Preventive treatment with isoniazid can be used in such countries; this treatment prevents tuberculosis from developing in infected persons. However, in developing countries with scarce resources which must be concentrated on finding and treating the large number of infectious cases, preventive treatment is usually not feasible or has very limited applicability (e.g., in young, close contacts of infectious cases).

Control methods include case finding, treatment, and use of vaccines. Case finding is not an end in itself; it is a preliminary to treatment and cure. Case finding and treatment form part of the same campaign against sources of infection. No purpose is served in expanding case finding beyond the capacity of health services to provide treatment to identified cases and cure them. Treatment should be free of charge and should be primarily ambulatory, which means it has to be decentralized.

Case finding should be carried out primarily and continuously among persons who have symptoms and of their own volition attend clinics. Most persons who are found to have bacteriologically confirmed tuberculosis are identified because they seek medical care for symptoms caused by the disease. In addition, persons already receiving care for another reason may be found to have concurrent tuberculosis. Thus, patients themselves and providers of primary health care are most likely to discover tuberculosis.

People must be taught to recognize symptoms of potential disease and to seek medical care when these symptoms occur and persist. Health care providers must be alert to the possibility of tuberculosis in a patient with prolonged cough, malaise, fever, and weight loss.

Only after the development of good countrywide diagnostic services for patients with symptoms should the examination of groups at special risk be considered. The most easily identified persons at high risk are contacts of newly diagnosed cases. Examination will be most productive among contacts of infectious (smear-positive) cases and especially among wuch contacts who are symptomatic. Fewer tuberculosis cases are identified through screening activities; screening, if done at all, should be highly selective among known high risk groups. Random, repetitive, routine mass screening is ineffective, unproductive, and expensive.

The importance of bacteriologic investigation of sputum cannot be overemphasized since the demonstration of tubercle bacilli is diagnostically conclusive. If treatment is initiated on the basis of radiographic findings alone, many patients are treated unnecessarily. This wastes resources and threatens the successful treatment of infectious cases.

Institutional treatment is irrelevant for the success of tuberculosis chemotherapy. Financial resources and manpower should be devoted to the organization of efficient ambulatory treatment programs. It is now known that the only absolute necessity for the treatment of tuberculosis is the actual ingestion or injection of effective antituberculosis drugs for the required period of time. Chemotherapy usually results in a rapid reduction of the patient's bacterial population and subsidence of symptoms. With fewer bacilli to excrete and disappearing cough, the patient quickly becomes uninfective. Therefore, physical isolation is not important and an early return to ordinary activities is possible.

Important considerations in the choice of primary regimens are efficacy, toxicity, acceptability, and cost. There are well established drug combinations and dosages based on results of controlled, clinical trials. Standardized regimens, selected to meet local conditions, should be used throughout the treatment network. The first priority in treatment is to obtain good results in treatment of newly diagnosed patients. Retreatment (reserve) programs for patients with drug-resistant organisms should not be attempted until it is clear that they will not drain available resources from priority activities. Retreatment regimens are more complicated, more toxic, and more expensive than initial treatment. Many new patients can be treated for what it costs to re-treat one old patient. The need for retreatment can be largely avoided by high levels of efficacy in original treatment.

Treatment failures occur because inappropriate regimens are prescribed because the patient fails to adhere to the regimen or because he does not stay on it long enough. Most treatment failures are due to interruption of medication. Careful supervision of oral drug schedules is necessary: these can be carried out by surprise checks of medications and examinations of urine to test for excretion of drug metabolites. Irregular adherence to drug regimens can be reduced and patient cooperation increased through convenient, flexible systems of health care delivered by pleasant, understanding, knowledgeable, and motivated personnel.

Fully supervised treatment administered on a daily or intermittent basis is a good alternative to self-administered regimens. Directly administered, intermittent chemotherapy is highly effective, has lower toxicity than daily regimens of the same drugs, has lower cost, and avoids undetected irregularity inherent in self-administered regimens.

The optimum duration of treatment is not known. It is undoubtedly influenced by such factors as the number and kinds of drugs used, the size of the bacillary population in the patient, and the patient's immunologic status. The ultimate goal of chemotherapy is to eradicate all viable tubercle bacilli from the infected host. Present forms of chemotherapy may not be able to achieve this ideal--even after prolonged treatment. However, the usually successful outcome of treatment along with the favorable long-term prognosis of treated patients indicate that chemotherapy alters the host-bacterium relationship sufficiently to achieve clinical cure. The benefits of prolonging chemotherapy beyond a year are small. Therefore, in developing countries, efforts should be concentrated on ensuring that every patient receives at least one year of chemotherapy without interruption. Regimens shorter than one year are being developed. Although still under study, accumulating evidence suggests that short-course regimens are going to be used on a very wide scale and that they will have a decisive influence on the organization of future programs in many countries.

Relapse after good chemotherapy is rare. Hence, less emphasis is placed on followup when chemotherapy is completed. Patients should be discharged after completion of the prescribed treatment with the advice to return if symptoms recur. They should not remain in the treatment network where they divert scare resources from new patients and patients still under treatment.

Administration of the attenuated bacillus of Calmette and Guerin (BCG) is intended to simulate natural tuberculous infection and produce an immune response which will protect against subsequent infection with virulent tubercle bacilli. BCG immunization does not necessarily prevent infection with virulent tubercle bacilli, but it may reduce the immediate complications of infection which stem from lymphatic or hematogenous spread, especially miliary tuberculosis and tuberculous meningitis.

There are many BCG vaccines in the world today. All are derived from the original strain; but they vary as a result of genetic changes in the bacterial strains, differences in techniques of production, differences in methods and routes of vaccine administration, and characteristics of the populations and environments in which vaccine has been studied. The vaccines now available differ from products used in controlled field trials in that many culture passages have since taken place, and there have been modifications in methods of preparation and preservation. The efficacy of these current vaccines has not been demonstrated and can only be inferred.

BCG may benefit uninfected persons with repeated exposure to infective cases who cannot or will not obtain or accept treatment. The value of the vaccine depends on its inherent efficacy, on the infection rate in the population, and the proportion of the population that is uninfected. In developing countries where the risk of infection is high, widespread use of BCG vaccine can play an important role in the tuberculosis control program.

BCG immunization is an adjunct to, not a substitute for, a case finding and treatment program; the need for an immunization program is an acknowledgement that the case finding and treatment program is not sufficient to effectively control tuberculosis in a given area.

In developing countries, most of the adult population is likely to be naturally infected; BCG vaccine then is aimed at the young. A feasible target in an initial, intensive mass campaign is the rapid coverage of 70-90% of the eligible population (usually all persons up to 15 or 20 years of age). To facilitate this campaign, direct immunization without prior tuberculin skin testing should be used. BCG does not benefit persons who are already infected, but neither does it harm them; an attempt to sort them out reduces the coverage and more than doubles the cost. After an initial mass immunization campaign, a program integrated with the general health services is more likely to achieve and maintain high coverage. Whenever justified and expedient, BCG should be given along with immunizations against other diseases by the same staff. Where infant tuberculosis is a problem, the widest possible BCG coverage should be ensured as early in life as feasible. Unfortunately, this is often difficult to achieve for infants born outside hospitals and not attended by health workers, particularly in rural areaa. Therefore, immunization at school entrance should also be a component of the program.

BCG has been associated with adverse reactions which include severe or prolonged ulceration at the site of vaccine administration and draining lymph glands. The reported frequency of complications varies greatly and depends in part on the extent of the surveillance effort. These complications may discourage participation in immunization programs and may, thus, affect the success of other vaccine programs which are combined with the BCG program.

After BCG immunization, it is usually not possible to distinguish between a tuberculin reaction caused by virulent superinfection and one that results from persistent post-vaccine sensitivity. Therefore, caution is advised in attributing a positive skin test to BCG, particularly if the reaction is large and the vaccine recipient has recently been exposed to infective tuberculosis. Tuberculosis should be included in the differential diagnosis of any tuberculosis-like illness even in a person who has received BCG vaccine.

In order to measure the prevalence and annual incidence of tuberculous infection, it is necessary to tuberculin skin test unimmunized children (i.e., those without BCG scars). In countries where vaccine coverage is poor, there may be an abundance of such children. This fact is in itself an admission of the difficulties involved in successfully mounting a mass BCG campaign. In countries with good coverage, especially at early ages, there may be few unimmunized children, and they may not be representative of all children in the country. In order to be able to use the tuberculin skin test as an assessment tool, it may be necessary to deliberately lease a selected sample of children unimmunized so that they can be skin tested later or to give BCG vaccine at a later age so that all children below the target age will be unimmunized and eligible for skin testing.

Implementing a Control Program

A national tuberculosis control program should be located within the Ministry of Health, should be administered centrally, and should have a strong directorate. The program should be initiated in one or a few areas and then extended to other areas as resources allow. The districts first included in the control program act as a testing ground and training school. It is in these areas that work methods are adapted to local needs and conditions. Here, also, evaluation begins so that schedules, procedures, and goals can be readjusted before they come into general use.

In the field, program implementation should be the responsibility of mobile managerial teams. These teams supervise program operations at the peripheral level; provide in-service training and retraining; check the condition of basic equipment (particularly microscopes); and ensure a regular and uninterrupted supply of drugs and BCG vaccine. They must help to set up a simple system of evaluation--based on standardized forms and registers--to be used for program monitoring and future planning.

Training of health service staff at all levels is important. Training is as necessary for those in charge of medical and paramedical services at the national level as it is for workers at the local level. At all levels, it is imperative that staff understand that community aspects of the problem take precedence over clinical aspects. Education and training should be program-oriented and practical. All personnel must understand the basic strategy and priorities of the control program. The key role in program implementation will be played by managerial teams consisting of physicians, bacteriologists, and administrators who must check performance, correct deficiencies, and provide in-service training.

Organization of laboratory services is a preliminary requisite for any attack on the problem of tuberculosis. Top priority is direct examination of sputum smears in peripheral laboratories throughout the country. The aim of a bacteriological service in a developing country should be to perform enough microscopic examinations of sputum to diagnose every smear-positive case and then follow the progress of therapy. Culture examinations, which should be made only in large, regional laboratories, will confirm the diagnosis of tuberculosis in an additional number of patients--mainly those who are not excreting large numbers of bacilli. These patients are of less importance epidemiologically in transmission of infection: their detection should not be attempted until a reasonably high proportion of smear-positive cases have been discovered and treated. The central laboratory plays a fundamental part in the organization of in-service training and retraining; in the choice and maintenance of laboratory equipment; and in the quality control of technical procedures used in regional and local laboratories.

Treatment consists essentially of ambulatory chemotherapy: the major problem is to ensure that patients receive their treatment regularly throughout the prescribed period of time. To achieve this goal, local treatment centers must have staff capable of explaining the treatment and its importance to patients and their families. It is necessary to be able to locate the patient by having his/her address and the addresses of relatives, employers, or schools. Staff members of each treatment center should be assigned to trace patients who fail to attend. Completely supervised, directly administered intermittent treatment should be used to the maximum extent possible in order to assure that medication gets into the greatest number of patients.

Once program needs have been defined, quantitative, measurable objectives and subobjectives must be established: these serve as the basis for planning and evaluation. These objectives must be realistic in terms of resources and feasibility. As an example, if a prevalence survey were done to estimate the number of infectious cases in the community and clinic records indicated that only one-third this number were under treatment, a numerical objective could be established to improve this situation in a specified time period. An objective to treat 100% of the estimated infectious individuals would be unrealistic; but it might be feasible to try to treat 50% in two years and 85% in five years. Achievement level is related to available resources, case finding and treatment procedures, and performance in the field.

Program evaluation should allow directors, supervisors, and peripheral staff to answer three basic questions: (1) To what extent were program objectives met? (2) How did the program's plans, resources, methods, and operations contribute to its results? (3) How should the program modify its objectives, plans, resources, methods, or operations in order to be more successful?

Surveillance is necessary initially to accumulate data with which to document the existence, extent, and distribution of the disease problem. Ongoing surveillance provides a continuous measure of disease occurrence or transmission. Thus, surveillance systems may indicate both the need for a program, and the extent to which the program influences disease mortality, morbidity, and infection trends. These data can guide the empidemiologist and the public health administrator by indicating whether tuberculosis is increasing, static, or declining. However, surveillance data should be interpreted with caution since many factors not related to program efforts--economic, climatologic, or industrial--may affect the occurrence of disease.

The benefit derived from any program can be meaningfully measured only if it is related to a relevant, epidemiologically well defined denominator. For instance, it is less important to know the number of cases under treatment than it is to know the proportion of newly diagnosed patients cured in relation to the number of new cases estimated to have occurred in a given period. The number of BCG immunizations given is not as important as it is to estimate the number of cases prevented through immunization, the proportion of the population covered, and the risk of disease in the eligible population. Information on program benefits (outcomes) provides the only true measure of its achievement of the ultimate goal--the elimination and prevention of tuberculosis. However, in order to identify what led to the observed results, successes or failures, management and operations assessment of all program elements is also necessary. An important part of program evaluation at all levels is reports of activities (processes), but activities are meaningful only if they are related to successful outcomes. Evaluation can determine whether a plan designed to solve a particular problem is being carried out; it must also be used to determine whether or not the plan is succeeding and why.

Several questions need to be answered in order to identify basic causes of program deficiencies. What is the overall organizational structure of the Ministry of Health? Where does the tuberculosis program fit into the structure? Within the context of the overall health plan and budget, what priority does the tuberculosis program have? To what extent is the program integrated into the general health services or combined with other programs, such as leprosy control and immunization; and how does this affect its operations and achievements?

If units in a number of different organizational locations have tuberculosis program responsibilities, are their relationships such that a coordinated approach to planning and operations exist? Are responsibilities and relationships within the tuberculosis network clearly defined and recognized at the central, field supervisory, and peripheral levels ? Are position descriptions written and used, and do they accurately reflect employees' responsibilities? Are salaries, work incentives, and opportunities for advancement comparagle with those of personnel in other programs; and are they recognized as being fair compensation for performance?

Are personnel given adequate supervision, and are performance deficiencies promptly noted and corrective measures taken? Are adequate cost accounting records maintained? In determining overall program cost, are both capital expenditures (e.g., microcropes, refrigerators) and recurring expenditures (e.g., salaries, drugs) included? Is there an established process to procure drugs and materials, and to assure even distribution of these items?

To a large extent, these are the same questions that must be asked at the beginning of a program in order to assess the existing situation.

Whether continuous or periodic, evaluation requires the orderly collection, consolidation, and analysis of pertinent data; and their dissemination to all who need them, particulary those in a position to take necessary corrective action.

The following questions should be asked about data collection. Are the types of information required, the format to be used, the periodicity of collection, and the channels of communication standardized and understood? Is the system simple? Collection of more information than can or will be used discourages those who are submitting reports and frustrates those whose job it is to analyze them.

Is it possible to say how each item will be used? Is there provision for submission of routine reports even in the absence of new cases? Absence of a report may mean there is nothing to report or may be a failure to report something; therefore, it is important to receive data from all areas even when no cases have been seen. Is there a system for control of reports? Late, missing, or improperly completed reports require prompt follow-up.

The purpose of data collection and analysis is not only to determine what is happening and why, but also to determine what can be done about it. Action is the logical followup of surveillance, evaluation, or assessment. Feedback is important because reporting sources may have little appreciation of the purposes or utility of reports submitted and, thus, lack incentive for continuing to provide data. Information fed back to the field allows workers at the peripheral level to compare local disease trends with other areas; reports progress of the campaign in which they participate; and provides a means of transmitting technical information as a form of in-service training. Information should also be relayed to others who need to know, such as government officials, civil authorities, and media representatives.

In evaluating programs, it is important to remember that events which may have nothing to do with program operations may nevertheless affect the outcomes. Changes in housing, nutrition, and socioeconomic status can influence mortality, morbidity, and infection transmission. Catastrophic events, such as war, drought, and famine, can result in mogration of people and disruption of normal life patterns. It is very difficult to measure the contribution of factors such as these to the success or failure of the program. What can and should be measured, however, are the performance of program components which are known to contribute to the success or failure of the program. With regard to tuberculosis in developing countries, the two most important components are case finding and treatment, and the use of BCG vaccine. Appendix 2 and Appendix 3 give how these components may be evaluated.

Appendix 1

STAGES IN THE DEVELOPMENT OF A CASE FINDING AND TREATMENT PROGRAM

A Logical Sequence of Priorities

Stage I

Develop facilities for examination by direct sputum smear microscopy for persons presenting with symptoms.

Develop facilities for adequate treatment for excretors of tubercle bacilli.

Cover entire country with conveniently situated facilities before expanding case finding.

Stage II

Promote increased awareness of respiratory symptoms in order to improve case finding. This is done by health education of the population and training of medical, paramedical, and auxiliary staff involved in health programs.

Follow-up(re-examine) patients with persistent symptoms but initially sputum-negative.

Examine contacts, especially if symptomatic, concentrate on those exposed to infectious (smear-positive) cases.

Provide bacteriological examination of patients who have had a chest X-ray showing possible tuberculous disease.

Stage III

Develop diagnostic culture facilities in order to improve case finding and monitoring of treatment.

Stage IV

Use reserve regimens for patients who remain consistently sputum-positive, provided that retreatment is not allowed to strain the resources.

Develop drug susceptibility test capability to aid in selection of retreatment regimens.

Appendix 2

BCG EVALUATION

What is the immunizing capability of the vaccine?
Vaccine quality can be checked by obtaining samples from all along the chain of distribution and sending them to the laboratory for assessment of potency. Field storage and usage conditions should be noted.

Is the correct immunization technique being routinely used?
Supervisors in the field should be responsible for training staff and checking their technique.

What is the coverage of the eligible population?
The right people should be immunized at the right time. This should be checked by scar surveys in the field rather than by submitted reports.

Other indicators of potency and coverage of immunization are:
the frequency distribution of scar sizes/
the percent of complications (abscesses, draining lymph glands, bad scars);
the percent of tuberculin conversions following administration of BCG; and
the incidence of tuberculous meningitis (this assumes reliable diagnosis and complete notification).

If potent vaccine is being properly administered, it is possible to calculate the number of cases prevented:

Example: Cases Prevented in 10 Years by Immunization of All Children Under Age 5.

Eligible population (from census)	500,000
Infected (from skin test survey)	2%
Susceptibles, percent	98%
Susceptibles, number	490,000
Coverage (from scar survey or estimate)	70%
Susceptibles covered	343,000
Disease incidence (from surveys)	1 per 1,000
Cases expected in 10 years	3,430
BCG efficacy (from trials, lab data)	50% reduction
Cases prevented in 10 years	1,715

Appendix 3

CASE FINDING AND TREATMENT EVALUATION

How many patients are being treated:

This is the prevalence (at a point in time) or incidence (over a period of time) of registered cases.

What patients are being treated?

This indicates the importance attached to finding and treating infectious sources, and allows an estimate of the number of cases of low priority and the number being treated unnecessarily (those diagnosed on clinical/radiological evidence only).

How are the patients treated?

Inspection of treatment records in the peripheral areas makes it possible to evaluate all the technical and organizational aspects of treatment: the therapeutic regimens employed and their conformity with program recommendations; the regular attendance of patients and the measures taken in the case of absence; the place and duration of any hospital treatment.

What is the outcome of treatment?

The number of failures, deaths, relapses, and lost patients gives information about the effectiveness of the treatment network.

AN EVALUATION OF CASE FINDING AND TREATMENT, AND ITS UTILITY IN MODIFYING PROGRAMS IN ALGERIA

The results of the chemotherapy program were evaluated by retrospective survey of patients one year after diagnosis; the survey was done in 1971 for patients treated between 1968 and 1970.

Bacteriologically Positive Cases 1 year After Diagnosis

Cases starting treatment	1,079	(100%)
Negative at 12th month	450	(42%)
Lost by 12th month	393	(36%)
Dead (from TB and other causes)	52	(5%)
Still positive at 12th month	51	(5%)
Survivors with no sputum examination at 12th month	133	(12%)

The real effectiveness of the chemotherapy program is measured by the proportion of patients who shift from positive to negative bacteriological status. Lost patients indicate the organizational efficiency of the treatment network; a high rate reflects organizational and motivational (patient and staff) shortcomings. Deaths, persistent positivity, and unknown bacteriological status reflect deficiencies in case finding, treating, and monitoring which requires correction.

Evaluation of Changes in a Diagnosis and Treatment Network

To assess the diagnosis and treatment network, focal surveys were made of patient status at a given point in time. Performance at different locations can be compared in this way and by repeating the surveys, the effects of program modification can be demonstrated as shown in the following table.

		1970		1973	
	Population	600,000		685,000	
	under treatment	1,261	(100%)	1,832	(100%)
WHO?	Bacteriologic positive	673- 505	(41%)	1,217- 1,096	(60%)
	No bacteriologic proof	168	(13%)	121	(6%)
	Extrapulmonary	588	(46%)	615	(34%)
HOW:	Non-standard regimen	26	(2%)	-	-
	First treatment	1,114	(10%)	1,689	(92%)
	Retreatment	121	(10%)	145	(8%)
WHERE?	Hospitalized	-	-	-	-
	Specialized clinics	1,255	(99.5%)	1,348	(74%)
	Nonspecialized clinics	6	(0.5%)	484	(26%)
PREVA-LENCE	Known cases/100,000	210		268	
	infection/100,000	84		160	

There has been an increase in the number of patients being treated. There has been an increase in the number and proportion of bacteriologic positive patients being treated. Use of nonstandard regimens and retreatment were reduced, and number of first treatment was increased. There was a shift to non-specialized clinics which indicates integration of the program into the health infrastructure. The increase in patient load was mostly pulmonary cases, and of those, the proportion positive increased from 75% to 90%. Hospitalization is not being employed because there is a functional ambulatory system.

If a survey showed 0.25% of the population were excreting bacilli in 1970, it can then be estimated that there were 1,500 positive cases in the population at that time, of which only 505 (34%) were known and on treatment; they comprised only 41% of the total case load, the rest were lower priority cases. In 1973, assuming that 0.2% were excretors (a decline of this magnitude, about 20%, was shown between two surveys in Korea in 1965 and 1970), there would have been 1,370 positive cases in the population. Of these, 1,096 (80%) were known and on treatment; they comprised 60% of the total case load. Despite this improvement, 20% of the positive excretors are still not being found and treated. This calls for further adjustments in the program. Who are these people and why is the program not reaching them?

In Algeria, the shortcomings of the program in rural areas became apparent. Even though the program in these areas was fully integrated into the general health services, lack of training and motivation of staff accounted for poor performance. Where non-specialized personnel were well motivated, results obtained were comparable to those obtained in specialized clinics in the urban area. This indicated a need for better training and supervision in rural areas.

The next step in this process of evaluation would be to repeat the survey of treatment outcomes to determine whether operational improvements resulted in a higher rate of sputum-negativity at 1 year, and a lower rate of patient loss before treatment was completed.

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VENEREAL DISEASE CONTROL

by

Merlin L. Brubaker

Throughout most of the world today, the incidence of sexually transmitted diseases is rampant. At least 14 different diseases transmitted by sexual contact (Table 1, page 85) can be considered venereal. Some of these are much more important than others either because of their extensive prevalence or the morbidity they produce. In most countries of the world, but especially developing countries, venereal disease means syphilis and gonorrhea. Less attention is devoted to the "minor" venereal diseases, such as Chancroid, Lymphogranuloma Venereum, and Granuloma Inguinale (Donovanosis). This paper will deal almost exclusively with syphilis and gonorrhea.

As with other common infectious diseases, the venereal diseases are poorly reported so that actual incidence is not known, perhaps not even suspected. This is especially true of gonorrhea in most countries of the world. Following World War II and the widespread use of sulfa drugs, penicillin, and other antibiotics, gonorrhea and syphilis incidence declined. After this apparent success, the medical profession, the public and health officials relaxed efforts directed against these diseases. Cuts in control programs in conjunction with marked changed in sexual activity patterns during the 1960's led to huge increases in these diseases throughout the world.

Syphilis and gonorrhea are the most important of the venereal diseases because of their prevalence. Syphilis is especially important because of its chronicity and the serious lesions, disabilities, and deaths that can result from it. Both diseases are transmitted from person to person by direct, intimate contact, usually sexual. The highest rates, therefore, are found in those who are most sexually active (persons aged 15-35) and particularly those groups whose pattern of sexual activity include numerous sex partners. These diseases constitute a major public health problem throughout the world in both developed and developing countries, but resources available for control programs are more limited in developing countries.

Control of these diseases is difficult because the only preventive methods available--changing sexual habits and attitudes or use of devices, such as the condom or protective foams, are only partially effective at best. Until an effective primary preventive tool such as a vaccine can be developed, the control of these diseases will remain difficult and relatively expensive because of the need for individual diagnostic and treatment services.

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Table 1

SEXUALLY TRANSMITTED DISEASES IN MAN*

	ORGANISM**	DISEASE
Spirochettes	T. pallidum	Syphilis
Bacteria	Gonococcus	Gonorrhea
	H. ducreyi	Chancroid
	Donovania	Granuloma inguinale
Viruses	Chlamydia***	Nongonococcal urethritis
		Lymphogranuloma venereum
	Other viruses	Herpes simplex
		Molluscum contagiosium
Protozoa	T. vaginalis	Trichomoniasis
Fungi	C. albicans	Monilia
	Epidermophyton inguinale	Tinea cruris
Parasites	Acarus scabei	Scabies
	Phthirus pubis	Pediculosis

* Adapted from: Wilcox R.R. A World Look at the Venereal Diseases. Med Clinics No America, 56(5):1059-1071, 1972.

** Other sexually transmitted organisms whose roles in relation to venereal disease are not yet clear include mycoplasmas, Diphtheroids, Haemophilus vaginalis, Mimeae (Moraxellac), Herrelea vaginocola, Cytomegalic virus.

*** These organisms were believed to be viruses, but they are now classified separately by Chlamydozoa.

Elements of a Control Program

The basic objective of a control program is to prevent or reduce transmission of the etiologic agents and, thereby, decrease prevalence, illness, and human suffering. A control program should include all of the elements described in the following sections. Compromises may be made in the degree of emphasis put into each element, though reduction in part or all of the elements beyond a certain degree due to lack of adequate resources will result in an ineffective program.

Initially, some idea of the scope of the problem must be established through the use of available data, a pilot study, or if necessary, special surveys of physician, clinic, hospital, birth and death records, or special screening surveys. At the start of the program, a single area can be selected where the problem can be defined with a fair degree of clarity and accuracy. Results obtained in the first area selected can be projected to comparable areas, and the size and degree of program commitment can be extended as reliable information becomes available. This means that a system for recording, reporting, and analyzing data must be developed at the start of the program. Data are necessary for program evaluation also. The process of data gathering and evaluation are continuous and the results of evaluation are used to correct and redirect program activities in order to meet program goals.

Clinical services are the foundation on which the total program rests: they include diagnostic, laboratory, and treatment services both public and private. The availability of these services needs to be assessed. In addition, the available services should be organized so as to provide information about disease occurrence among population subgroups and disease trends. Additionally, these data should be useful in evaluating the effectiveness of care offered. The clinical laboratory is a vital, integral component of diagnostic capability: it also allows for a very important component of the program--mass screening for undiagnosed disease.

For every new case diagnosed, the individual who was the source of infection and all contacts to the case should be found and treated to prevent the effects of the disease and its spread to others. Contact follow-up indices, i.e., number of contacts per case, number of contacts found and brought to treatment, etc., serve the case finding component of the program as well. Case finding should also include mass screening programs (serological tests for syphilis and cultures for gonococcal infection) to find unsuspected and undiagnosed disease. Routine serological tests for syphilis and treatment when appropriate as part of physical examinations for workers, students, police, the armed forces, in maternal and child health clinics, in family planning clinics, etc., can lead to a reduction in morbidity and the reservoir of infection.

Screening for gonorrhea presents a greater problem, but is necessary if cases are to be found early, treated, and the spread of disease prevented. Screening can be especially effective since it has been observed that as much as 80% of females and 15-30% of males with positive gonococcal cultures are asymptomatic. Cervical culture on Thayer-Martin Media should be obtained as a screening procedure as often as practical as part of prenatal, family planning, and other gynecological examinations in those groups where the potential for unsuspected infection is high.

Education is an equally important component of control; it should be directed at the patient, the general public, high risk groups in particular, and health professionals. Education should begin, however, with professionals for their attitudes will determine to a large extent the eventual success of the program and its acceptance by the staff and the public. Professional education about sexually transmitted diseases should be part of every health profession curriculum and should include careful consideration of the development of appropriate attitudes in the professional as well as provide the technical basis for diagnosis and treatment of the disease

The program data which are collected can provide a continuous basis for evaluating the success or failure of the program effort and point to the changes necessary for improvement.

Planning a Program

The information included in this section is intended to provide useful ideas for planning and maintaining a VD control program. To what degree these components can be incorporated into a given health structure depends on the resources, financial and human, that are available locally.

However, before implementing control measures, health planners must first determine the degree to which syphilis and gonorrhea are prevalent in the population.

An effective way to initiate program activities is to utilize a study group appointed and sanctioned at the highest level of government. This study group should include experts in the fields of medicine, epidemiology, statistics, and national culture; it should be convened for a period of time adequate to gather and analyze available data. Analysis may be confined to a single geographical area; the findings can then be projected with caution, to similar or contiguous localities. Recommendations made by the group will form the basis for the direction and extent of the control program.

An understanding of the potential for the spread of syphilis and gonorrhea within the society is of prime importance. The complex anthropological-social determinants of a culture dictate its sexual mores. The study group will be aided greatly by knowing the age at which sexual intercourse is first practiced; whether in a monogamous or polygamous context; if prostitution is widely practiced and to what extent patronized; to what degree these customs differ between rural and urban settings; and the influence religion and other cultural factors exert on the population to shape sexual behavior.

Additionally, the study group must have at its disposal a wide range of demographic data. Comparisons should be expressed in terms of rates per 10,000; 100,000; or 1,000,000 population. Beyond the commonly used variables such as age, sex, median income, etc., information about health practices within the community is needed.

What proportion of the population is served by government (public) health facilities? Do patients seeking care discriminate between different health units? Do they utilize venereal disease clinics? More than likely, the decision to establish a control program is the result of the actual or presumed presence of these diseases. Few developing countries have laws which specially mandate the reporting of syphilis and gonorrhea or, if they do, have probably not rigorously enforced them. Nevertheless, the study group should request any such reports received by the ministry of health. These reports are a starting point to help determine the scope of the problem as well as the facilities at which these are diagnosed and treated. If case reports are too few or unreliable, an estimate of disease incidence can be obtained from medical records. First, the most important treatment facilities (clinics, hospitals, physicians) are listed by size, type of patient served, laboratory proximity, and quality of medical record information. A random sample of patient names should be drawn from an annual roster if available. If not available, a random sample of patient records for those known to have been treated during the period of interest will be suitable. However, when a study sample is drawn from patient visits, the sample will be biased because patients with more frequent visits will be over represented. The study should encompass a review of the past several years to facilitate the identification of trends. The review process will enable the study group to determine the validity of diagnostic and laboratory procedures.

International agencies, as well as other large, nationally oriented programs (family planning, nutrition, infectious disease) also represent excellent sources for documenting disease levels. They can offer invaluable insight into population segments seeking specialized, rather than generalized, services.

Throughout the information gathering phase, group members should continuously plot all findings geographically and relate them to known demographic data for a specified area. This will provide a visual delineation of "hot bed" areas and, also, define the characteristics of that population group.

The next step after completion of the data collection phase is to check the reliability of any estimates that have been made. This can be accomplished through the rapid screening of specific groups. It is important to include persons whose characteristics resemble those studied as part of the medical record review procedure. Reliable laboratory tests include the Rapid Plasma Reagin (RPR) and Venereal Disease Research Laboratory (VDRL) tests for syphilis, and Gram's stain smear for males and cultures for gonorrhea. Screening, both general and within specific age groups, should be carried out in those geographical areas where risk is high. The screening of prostitutes may be an excellent method to measure prevalence in those countries with widespread prostitution. Check stations may be established at points where people congregate (market places, ferry crossings) in nations with a mobile population.

Demographic information should be collected for all persons tested. Information collected during assessment on persons infected with syphilis can be used as the basis for establishing a central registry file.

As reliable information becomes available, the study group findings should be adjusted. Re-evaluation must be dynamic--not constrained or molded by preconceived views. Comparisons with statistics from other countries should be made with great care, and conclusions should be drawn only after consideration of all important factors.

Reports of syphilis and gonorrhea morbidity as well as positive laboratory results are critical to the efficacy of the control program. Study group members should identify and, whenever possible, utilize existing reporting systems, e.g., air mail, personal courier, boats, rather than try to establish new ones which may be both costly and difficult to achieve. Even if control is initially concentrated in one area, morbidity reporting should be encouraged throughout the country.

Accumulated data are more useful when maintained in a central location. This facilitates disease surveillance and statistical evaluation. Since the prevention of sequelae of syphilis is a major objective of any control program, it is suggested that syphilis morbidity records be kept for a minimum of 20 years and constantly updated with new serologic results or reinfection data. Whenever possible, disease diagnosis should be confirmed. Individual gonorrhea morbidity reports, once analyzed and summarized, may be destroyed unless epidemiologic follow-up is planned.

Disease notifications should be analyzed by reporting source in order to determine the degree of private physician participation in the control program, to estimate the amount of underreporting among private practitioners in various areas, and to plan program efforts necessary to stimulate more active participation by physicians in syphilis control.

In making their recommendations, the study group must consider many factors. They must consider the extent of the problem as suggested by the data accumulated and if the data are reliable. Then they must decide if control is realistic among the majority of residents in view of social and cultural characteristics. They must also estimate if experienced personnel are available and if sufficient governmental interest exists to proceed with the control program.

Budgetary considerations must be weighed: the expectation of future financial support is critical. Will budget appropriations stay abreast of changing program needs?

Is the communications system conducive to a centralized organizational structure? The control of gonorrhea and syphilis require the rapid interchange of information; without reliable communications, control efforts will be greatly hampered.

As an alternative to a national program, the group may consider a small demonstration project. In a small project, the best components of a venereal disease control program can be incorporated and evaluated accordingly. This will also minimize the burden of stretching resources beyond a country's ability to do so. Once the program has been operational, similar programs can be "transported" to other urban centers around the country.

The area selected for the project must possess the following features:

a high level of morbidity;
an adequate medical facility which offers laboratory support;
a public transportation system;
a good communications system.

Having settled on a course of action, the committee must define its objectives. Plans for more than a year may be meaningless as experience during the early stages will alter program emphasis and direction. The objectives should encompass as many of the control elements as possible, but the group must decide what they can achieve based on available resources and trained personnel.

Elements of a Control Program

The technology available for disrupting the spread of syphilis and gonorrhea is centered around the rapid and effective treatment of persons infected with or suspected of having syphilis or gonorrhea. All control program components are geared toward a single goal: detection of as many individuals as possible during the early stages of their disease.

A well-organized, well-administered clinic is the essential ingredient for any successful control program. It is the center at which treatment is given to persons infected with syphilis and gonorrhea. It should be centrally located and near public transportation. It is important that it be accessible to the working public during evening hours. The staff needs to be thoroughly trained and familiar with all major sexually transmitted diseases as patient problems may not be confined to gonorrhea and syphilis alone. Above all, the clinic must never project a moralistic attitude.

There should be a spirit of partnership fostered between the clinic and the private medical sector. This is especially true if data indicate widespread utilization of private medical care. The private sector should freely refer their patients to the clinic for rapid laboratory tests and other diagnostic aids. On the other hand, physicians can enhance this relationship by giving permission for epidemiologic follow-up of their patients by staff at the public facility. Physicians must be encouraged to report all disease diagnosed to the control program central registry.

The clinic should be the trend setter, the center for expertise in diagnosis and treatment. It should carry out drug efficacy studies, serologic studies, and other surveys as needed. Clinic personnel should continuously monitor disease trends both in high risk groups and among geographical areas. The information obtained should be reported to national authorities.

Obviously, the most important role of the clinic is providing a service. Patient management is, therefore, of prime importance. Patient flow should increase accessability, decrease waiting time, and leave the patient feeling that he is being handled professionally. Every effort must be made to insure that patients are never turned away.

All patients should be referred back to the clinic one week after treatment to be advised of VDRL and culture test results. It is important that the clinician note symptom response to treatment, as well as any adverse reaction, such as allergy or Herxheimer reaction, experienced by the patient. Ideally, female gonorrhea patients should receive a test-of-cure endocervical and rectal culture, swabbed on separate plates. Males may receive a erethral culture; but if a discharge is present, should receive an immediate gram stain. Other sites are to be cultured if they were originally positive prior to treatment.

All patients should be given an appointment to the clinic for a follow-up VDRL and gonorrhea culture examination every three months if local capability and resources permit. Guidelines for gonorrhea tests may follow those given above. An anorectal culture is recommended for all known and suspected homosexual patients.

To provide the services outlined above and to verify clinical impressions, full laboratory capability is essential. The following is a brief summary of the basic tests performed for the diagnosis of syphilis and gonorrhea:

Syphilis:

Examination of lesion material: Early syphilis lesions should be examined by use of a darkfield microscope if available locally or by use of the fluorescent antibody technique if tests need to be delayed. Lymph node aspiration may be indicated.

Reagin test of blood specimen: 6 to 10 ml. of venous blood should be collected in a sterile vial. Reagin tests turn reactive 3 to 6 weeks after infection. A fourfold titer rise on subsequent tests is evidence of a new infection.

Reagin and protein test on spinal fluid: 25 ml. of spinal fluid uncontaminated by blood should be collected in a sterile vial. A cell count must be done within several hours; other tests can be delayed.

Teponemal tests: a specimen is collected as for the reagin test and noted for Fluorescent Treponemal Antibody (FTA) or Microhemogglutinatin Treponema Pallidum (MHA-TP) test. These tests help rule out biological false positive reactions that are sometimes obtained with the reagin test. They may also be used to confirm the original diagnosis but are not valid for assessing response to therapy as they may remain positive indefinitely.

Gonorrhea:

Gram's stain: N. gonorrhoeae are identified as gram negative intracellular diplococci. This test is an excellent tool for identifying gonococci from male urethral secretions in the presence of an abundance of organisms. It is not recommended as a diagnostic test for samples from the rectum or from women.

Culture examination: This examination utilizes an oxidase test or the fermentation reaction method to carry out definitive tests on samples that have been grown on various types of transport media. In all cases, a positive culture is diagnostic for N. gonorrhoeae.

As pointed out previously, achievement of a high level of VD control depends upon the provision of well-organized, specialized VD diagnostic and treatment services, especially in nations with high syphilis and gonorrhea rates. However, good clinical services alone will not insure success. Medical care and follow-up must be administered in tandem with a routine and aggressive contact follow-up system. Treatment services directed solely at the index case without a search for infected and potentially infected contacts will do little to halt ever increasing venereal disease incidence.

In the absence of a vaccine, the only available control method is through the rapid treatment of known cases and prevention of disease spread to their contacts. The method used to accomplish this is the contact interview. All sexual contacts and other associated persons elicited through this interview are directed to a treatment facility for medical evaluation.

The contact interview has two purposes--case finding and case prevention. The success of this follow-up process is determined eventually by identification and treatment of the source (for the original infection) and the secondary cases. Success is preventing the future occurrence of venereal diseases in the population will depend increasingly on the number of contacts, especially those exposed directly during the infectious stages, that receive prophylactic treatment. Although the basic principles involved are simple in theory, they are difficult in practice because of the human element and they require individual worker resourcefulness, imagination, and determination.

Case finding and contact follow-up services are more effective when organized into a special unit with staff sufficient to carry out interviewing and contact tracing activities. All case reports from public, private, and government agency sources should be directed to this office for appropriate action. Ideally, this unit should be located within or near the major diagnostic center where the majority of VD cases receive treatment.

At a minimum, intensive contact follow-up should be applied to every diagnosed case of primary, secondary, or early latent syphilis of less than one year's duration since these cases become infectious after relatively long incubation periods. Primary syphilis cases should be interviewed to elicit contacts for a maximum (incubation) period of three months plus the duration of symptoms. Secondary syphilis cases should be interviewed for sexual contacts during the preceding six months plus the duration of symptoms. Patients with early latent syphilis should be asked about sex partners for the entire year prior to treatment.

Since gonorrhea has a much shorter incubation period than syphilis, the interview should be confined to requests for information about sexual contacts within the previous 30 days plus the duration of symptoms. Depending on manpower resources and clinic space, interviewers should concentrate attention on the infected male as a means to identify the asymptomatic infected female. If case loads are heavy, gonorrhea patients may be given self-interview forms and asked to list their contacts. This technique is less embarrassing for the patient and frees interviewers for other duties. Self-report, however, is not as effective as a personal interview in eliciting contacts.

Female gonorrhea patients, if not interviewed, should at least be instructed to refer all contacts for examination regardless of whether or not they are symptomatic. Patients should be told to avoid contact with any sexual partner who has not been examined in order to avoid reinfections.

Every patient treated for a venereal disease, whether in the public clinic or by a private physician, needs to be given basic information. He/she should understand the manner in which the infection was acquired, how it is to be cured, the necessity to return for follow-up medical examinations, and his/her role in preventing the further spread of the disease through contact identification.

A good interview is based on an organized plan. Interviewing success depends upon the interviewer's ability to control the conversation and motivate the patient through positive attitudes and responses. This projection is accomplished by the use of positively phrased questions and overtones which indicate concern for the patient and his/her problem. There should be an attempt to develop rapport. The interviewer must never give the impression that he/she is making moral judgments. Most important, the interviewer must have sound reasons when asking his/her questions.

All cases interviewed should be given a reinterview appointment, preferably within a week. In the interim, the interviewer has time to review the original information and decide what items need further clarification. It is best to begin contact investigations before the reinterview in order that inconsistencies may be clarified with the patient.

As an adjunct to the contact interview, widespread mass screening should be encouraged as a means to broaden case finding capability. A test on blood specimens for syphilis and a smear and culture for gonorrhea can be recommended as part of routine examinations. Gonorrhea screening is more fully discussed below in Section 4.

Routine serologic tests will result in the detection of most cases of syphilis. Screening should be encouraged as part of every hospital admission, employment or military physical, prenatal, family planning, maternal and infant clinic examination, and should be included at other places where large population groups are examined. Although screening should be emphasized for those in sexually active and at-risk groups, it certainly need not be limited to such persons. If screening is limited to persons aged 15-35, many older people infected with syphilis will be missed.

Health education involves a process that attempts to alter personal health practices by changing associated knowledge and attitudes. In addition, health education places responsibility on the individual through motivation, communication, and decision making. In the case of the sexually transmitted diseases, education contributes notably to their prevention and control.

Venereal disease education attempts primarily to create a basic awareness of sexually transmitted diseases among a variety of population segments. Although the message may vary, the intent is the same: to motivate people so that they seek rapid medical care for themselves and their sexual partners.

Provision of VD information to private physicians is paramount to any control effort. In many countries, they are the major source for VD treatment and as such need to be kept abreast of current diagnostic and therapeutic recommendations. Professional journals, medical association meetings, mailings, and personal visits are direct means for providing this information to them. Material should be designed to increase their index of suspicion to the possibility of infection among their patients, make them knowledgeable enough to make accurate VD diagnoses, and persuade them to report their cases. The physician should get the message that they are playing a key, if not decisive, role in disease control; that their goals and those of public health must be the same.

In those countries with medical schools, officials should ascertain the quality of information, both technical and attitudinal, taught the student. By intervening early in these training programs, it is possible to raise the level of interest these physicians will demonstrate in the future. An excellent training program officials can establish is one that rotates students through the VD clinic as part of the medical school curriculum. This not only aids in the development of appropriate attitudes, but provides job skills and an exposure to public health personnel and their methods.

It is also helpful to encourage the development of an information dissemination campaign for the general population. Of special value is use of the mass media as the most effective way of reaching the greatest number of people with a limited amount of resources. Media outlets that are available include: use of the newspapers for articles or special interest stories; radio and television (in prime time slots for maximum effect); magazines;

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and public display areas (buses, billboards, taxis, etc.). However, information campaigns that seek to encourage general audience turnout for VD examinations must be planned with a realistic assessment of local clinic diagnostic and treatment capability for handling large numbers of people.

Surveys reveal that TV and radio are especially productive. Messages should be short and arouse public curiosity for more information. They should be aimed at high-risk groups (youth and young adults, homosexuals, etc.).

Many developing nations have large illiterate populations in remote localities for which this type of mass media approach will be ineffective. An alternative approach is to form cooperative agreements with other health or voluntary agencies presently working in these areas, to integrate and disseminate VD information as part of their services. The message should be simple: how to recognize symptoms and where treatment can be obtained.

Clinics that offer VD services represent one of the best source for distributing VD information among high-risk segments of the population. Every effort should be made to intervene in the possible reinfection of patients. Oral and written information ought to stress control and prevention, recognition of signs and symptoms, complications and their consequences, and the need for adequate treatment. The clinician, the nurse, and the epidemiologist can all impart various items of information at each step of the clinic routine. Teamwork is important.

Venereal disease affects the young in overwhelming numbers and early knowledge promotes prevention. A school education program should be designed to:

integrate VD information as part of such courses as health education, biology, and physical education;

provide teaching aids (VD teachers manual, audiovisual aids);

increase the understanding of teaching needs and objectives on the part of school officials through inservice training.

Equivalents of parent-teacher associations when they exist, as well as other civic organizations, can be utilized to assist in promoting acceptance of classroom VD education. The school nurse or someone in a similar role is in a unique position to disseminate VD information. She is in daily contact with the students and can provide ongoing information through a variety of means that otherwise are underutilized.

Bringing together civic, service, professional, religious, and other governmental and unofficial organizations, agencies, community leaders, and individuals is an effective way to combat VD at the community level. Such an alliance of interested parties is an effort to resolve local VD problems through citizen involvement. Areas to which the energies of the alliance can be directed include:

Coordinating local regional, and national organizations' VD efforts.

Compiling data about and providing evaluation of community VD programs.

Working toward the adoption of legislation and regulations necessary to improve VD control.

Seeking private funds or donations to carry out special projects in conjunction with VD control.

The need for thorough gonorrhea surveillance has become even more urgent in view of the threat from penicillinase producing N. gonorrhoeae infections. It is critical to establish systematic and intensive screening projects throughout the control area. This may be done in conjunction with the demonstration project discussed earlier or at selected public and private health facilities serving high risk population groups. It is not enough to identify unknown, asymptomatic infection. It is, therefore, most cost effective when aimed primarily at females in their reproductive years. Program emphasis, however, may be directed at women under age 35 since the majority of the diagnosed cases fall in that category. Of course, the age range in which most cases occur may vary between countries. Screening for asymptomatic infection among males is most productive when limited to male sex partners of asymptomatic female cases.

Initially, three steps must be considered when establishing a gonorrhea screening program. First, financial resources must be determined. Equipment and screening materials will probably have to be supplied to each participating facility. Special laboratory report forms will be needed to aid in the identification, reporting, and evaluation of specimens. Personnel salaries must be computed. Knowing the level of funds that will be available, both on a short term and long range basis, will determine how extensive the activity can be.

Secondly, the degree of participation by the central laboratory should be ascertained. Limitations in physical space as well as shortage of adequate staff may affect their commitment, which is critical to the entire effort. It is recommended that the central laboratory prepare and monitor for quality control a suitable culture transport media as it may not be possible to purchase it commercially.

Thirdly, there must be a reliable, daily pickup and delivery system to transport fresh and innoculated specimens from participating screening centers to the laboratory. This factor alone generally limits screening to the major metropolitan centers.

Selection of health sites to participate in the screening activity will depend on a variety of factors: whether they serve patients considered to be in the high-risk groups; their anticipated volume of activity; proximity to the courier pickup system; interest in the project, etc. In the absence of reliable reporting patterns, attention may be directed to large facilities serving young women. These include family planning, maternal and child care, and other clinics.

In the areas of high disease incidence, screening services can be set up in the offices of cooperative physicians, in youth recreation centers, work camps, on or near military installations, prisons and other select locations. This is also an excellent opportunity to encourage routine syphilis screening via VDRL tests.

Proper training of health provider staff is essential to an efficient screening operation. Venereal disease control staff need to visit each health provider periodically to observe the technique utilized in taking and innoculating culture specimens. Reviewers must continually check on minute but important details such as (1) are media properly refrigerated; (2) are media plates kept free of contamination; and (3) are media used prior to expiration dates.

The provision of treatment for culture positive women and their contacts is of fundamental importance in preventing new cases as well as suppressing existing ones. All patients diagnosed with gonorrhea should be given an appointment to return one week after completing treatment.

At this time, a follow-up culture should be obtained to see if treatment has resulted in cure.

All post-treatment positive cultures, in the absence of reliable reinfection data, should be considered as possible cases of penicillinase producing N. gonorrhoeae (PPNG). When available, such cultures should be verified with a specific test for this infection, such as the rapid idiometric, acidometric, or chromagenic cephalosporic test. Nations that undertake screening activities need to be constantly aware of the threat of these infections. Special vigilance measures that may be adopted include:

Alert all health providers to the possible existence of PPNG among their patients.

Emphasize the importance of one-week post treatment follow-up cultures.

Advise all gonorrhea patients to return to the clinic if their symptoms persist after treatment.

Advise any patients with a negative culture, but especially those patients from or in the endemic areas to return for a re-check examination.

Maintenance of an effective screening component involves constant evaluation. All health providers need to be reviewed routinely and recommendations made to those who demonstrate difficulties. In the absence of measureable progress within a specified time period, such providers should be eliminated. It is imperative that screening be pursued among those age and other population subgroups defined to be at greatest risk for gonorrhea.

Reactor surveillance is defined to be the organized collection of positive serologic syphilis test reports from laboratories, private physicians, and pathologists in order to detect untreated or unreported cases of syphilis. This goal can best be accomplished by initiating a follow-up program which assures that all reactive or weakly reactive serologic test results and all positive darkfield examinations are reported to VD control officials. Also, all positive reports are to be accompanied by a medical disposition (morbidity report) or the physician's permission to refer these persons to a treatment facility.

Compliance with these requests will probably be haphazard at best. Because of laxity and the belief by many laboratory directors that reporting to public health authorities constitutes a breach of patient confidentiality, it may be helpful to pursue the adoption of a law or regulation that clearly establishes these responsibilities.

To measure laboratory compliance, it would be helpful to include in the regulation requirements that each laboratory keep an up-to-date record of each test processed and the results; that each laboratory submit yearly reports to the Control Program of total serologic tests performed and their results; and that laboratory records be accessible to review by health officials.

All reactor reports should contain the following information: patients full name, address, age, and sex; physician's name, address, and reason for requesting the test: the date, type of test; and results of the test. This information will facilitate record searching in the central registry file for previous morbidity history. It will also be the basis for follow-up.

Adoption of a law will not in itself guarantee successful reporting. To enlist the cooperation of each facility in the control area, program officials ought to visit every laboratory personally. These visits are an opportunity to explain the principles of the reactor program: misunderstanding will lead only to ineffective control. The following are some of the points that can be emphasized:

> Reports of positive reactors sent to the control program do not represent a morbidity report or a medical decision.
>
> Reporting is not meant to challenge the physician's authority but simply to provide an additional service.
>
> Confidentiality in all matters will be scrupulously observed by the control program.
>
> The proper method for completing the report forms and the reasons for a reporting law.

The control program will need to establish a method for follow-up of positive tests reported through this system. All reports must be searched through the central registry file; if a record is located, the information is updated. If no record is found, the new information is to be placed in file. In developing countries, a truly complete central registry file will develop only as more and more persons in the disease reservoir are identified.

If evaluation of a report indicates the necessity for field follow-up, the epidemiologic staff must be notified. A special investigative form will need to be developed for this purpose. It should contain the essential information submitted with the original report and a space for the final diagnosis and disposition. This information should similarly be added to the morbidity file in the registry.

In any control effort, certain test results require priority over others. With respect to syphilis, all reports of positive darkfield examinations should be given immediate attention and follow-up. High serologic titers in young persons or among persons in specific high-risk groups should be considered second in importance. All other persons with high titers are of lesser consequence, followed by persons with low or weakly reactive test results.

Evaluation

Complete and ongoing assessment of the control program is essential if health planners are to measure its impact on disrupting disease transmission. From the onset, all related documents, records, and reports must be used to establish baseline data. These data are the information source for setting objectives; in turn, new data must be fed into the review system to document the degree of achievement in meeting the stated objectives. Objectives should always be realistically attainable with local resources and be measureable.

The use of statistics is critical to program evaluation. Long-range plans cannot be updated without knowing program accomplishments since the problem was first documented. Compilation of statistics should be designed to continually update the level and scope of the problem as well as determine where modifications and refinements are needed to perfect control techniques.

The morbidity report form is the key document available for information collection and interpretation. It establishes disease incidence and prevalence; pinpoints high risk disease areas by specific geographical locations; and is used for projecting trends for planning purposes. Morbidity reports provide descriptive information by defining patients at risk by age, sex, and race, while noting fluctuations that occur among subgroups. They are also instrumental in measuring private physician participation in the control effort.

Evaluation, both quantitative and qualitative, should be carried out continuously and be presented in a consistent format for comparison purposes. Information summaries, statistical trends and indices should be continually fed back not only to program personnel but to the public and private sectors.

Statistical evaluation is of particular importance in the search for disease control funds. Such reports provide supportive evidence of program needs, i.e., additional personnel in a high disease geographical area. Progress reports should be prepared at regular intervals to show that funds are being directed at specified program goals and are achieving the desired results.

Data collection is also helpful in measuring an individual worker's strengths and weaknesses. Continuous review of an employee's indices of performance will help determine his/her potential for progress within the program. Collectively, these reports show the amount of time applied to priority work as opposed to work of lesser importance and, thus, can be used as a basis for shifting staff to areas of high disease incidence to equalize work loads.

The sexually transmitted diseases, although grossly underreported, are, nevertheless, the most commonly reported diseases in most countries of the world. Many, indeed most of these diseases go unreported to health officials, all too often go undiagnosed and, thus, finally lead to serious complications, disability, and even death. The degree of sophistication of the health system of a country will determine how often all 14 sexually transmitted diseases will be diagnosed and treated. Syphilis and gonorrhea, both because of their frequency, morbidity, and complications lead the list in importance for developing countries.

Control of these diseases is possible, but only if certain program components are implemented and adequate effort put forth. This entails an organized program, the necessary resources (human and material), political support, and power to accomplish the task. A control program for syphilis and gonorrhea has been described. All the elements of the program must be included; and compromise, often necessary where resources are limited, must be held to a minimum if effective control is to be achieved.

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BACTERIAL ENTERIC DISEASES

by

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The incidence of bacterial enteric diseases in developed countries has declined markedly over the past century due primarily to elevated standards of environmental and personal hygiene. In contrast, enteric diseases still constitute major public health problems which cause extensive morbidity and mortality in most developing countries. In these countries too, diarrheal disease is found in conjunction with widespread malnutrition: the combination is lethal and exacts its greatest toll among infants and preschool children.

Since the symptoms of many bacterial enteric agents are similar, diagnosis of the specific etiologic agent depends on laboratory tests that are not routinely available, even in developed countries. However, treatment of severe enteric disease (i.e., diarrhea) is almost entirely focused on rapid rehydration, regardless of the etiology. Thus, a simple public health strategy is available for the reduction of mortality due to diarrheal diseases. This paper will describe the characteristics of bacterial enteric diseases that may be measured and what may be achieved in control efforts based on such measurements.

Description of Common Bacterial Enteric Diseases

Shigella. The shigellae are among the most frequent bacterial causes of diarrhea in preschool children in developing countries. This group of organisms has four species: S. Dysenterii, S. Flexneri, S. boydii, and S. sonnei. The first three species are further subdivided serologically into many numbered types. Shigellae are host specific for man and are most frequently transmitted from child to child. Only a few organisms are necessary to produce infection in the host. Partial immunity to a particular type develops in individuals once infected; but, it may take many reinfections with the same type before acquired immunity prevents disease. Clinical shigellosis is often serious and protracted. Infection with Shigella is a prime cause of dysentery, a febrile illness characterized by sudden onset with abdominal pain and passage of frequent stools, containing blood and mucus, accompanied by tenesmus.

Antibiotics are helpful in therapy of the acute, serious illness, though their use is unnecessary for less serious illness.

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Many shigellae have developed resistance to the most commonly used antibiotics--a phenomenon noted throughout the world, most often in developing countries. Although an oral vaccine has been developed for some types, many doses of the vaccine must be given before significant protection results. Furthermore, protection is effective only for the serogroup and subtype for which the vaccine has been developed. Attempts continue to develop better vaccines, but none are yet available for routine use.

Although occasionally common source outbreaks of Shigella are associated with food or water, the variables most strongly associated with infection are age (the period of weaning), family size, lack of water for hand washing, and low income (Tables 1 and 2, page 102). The diagnosis can be confirmed by stool culture, although clinical findings of blood in the stool, fever, and laboratory identification of many white cells in fecal smears are suggestive of Shigella. Persons with shigellosis are frequently misdiagnosed as amebiasis since the white cells seen on fecal smears are confused with ameba. In areas in which Shigella infection is frequent, many children (up to 10%) may be culture positive even without disease, perhaps because of prior infection and resultant immunity. The least expensive diagnostic tests are not specific; confirmation can be made by use of stool culture, but that is expensive.

Escherichia Coli-Enteropathegenic (EPEC), Enterotoxigenic (ETEC). These constitute a large group of enteric bacteria which are often associated with diarrheal illness in children and adults, particularly in developing countries. These bacteria are also an important cause of travelers' diarrhea. Disease with E. coli has been associated with a variety of pathogenic factors, most recently with the ability of the bacteria to produce toxins or to penetrate into the gut. There are a group of E. coli described as enteropathogenic (EPEC) whose mode of disease production may be toxins or other mechanisms which remain unclear still. E. coli are characterized biochemically and serologically, and the number of serologic types is described by letter and number based on three separate antigenic groups. As a result, agents may be described by O, K, and H antigens, with each set of antigens described numerically--such as E. coli O111, K58, H12. Some E. coli serotypes have often been associated with enteric disease, while other serotypes are rarely associated with such diseases. Clinical illness associated with E. coli infection is variable and, perhaps, depends primarily on the pathogenic mechanisms of disease production. Illnesses range from mild afebrile diarrhea to those indistinguishable from cholera and may be brief or prolonged. Antibiotics are often used in treatment, although as with Shigella, antibiotics may be effective only in reducing the period of bacterial excretion without affecting the course of the illness.

Infections with E. coli are most frequent in preschool children, and the mode of spread may be similar to that of Shigella. The dose needed to initiate an infection is variable but may be large. At the present time, no vaccine is available to prevent infections with these organisms, but efforts are being made to develop a vaccine to those which are toxigenic. Diagnosis is made entirely by culture and further study of isolates since the

Table 1

SHIGELLA POSITIVE CULTURES FROM SYMPTOMATIC CHILDREN BY AGE

THREE COMMUNITY SURVEYS

Age (Years)	Guatemala (1955-56)			California: Camps (1950)			Egypt (1953)		
		Positive			Positive			Positive	
	Cultures	Number	%	Cultures	Number	%	Cultures	Number	%
1	182	5	2.7	532	19	3.6	1,064	59	5.5
1-2	202	24	11.8	455	40	8.8	1,423	125	8.8
2-4	734	63	8.6	1,408	86	6.1	3,021	203	6.7
5-9	1,224	83	6.8	1,130	72	6.4	-	-	-

Source: Diarrheal Disease with Special Reference to the Americas.
Verhestraete, L.J., Puffer, R.R., Bull WHO, 1958.

Table 2

ASYMPTOMATIC CHILDREN WITH ENTERIC BACTERIAL PATHOGENS BY AGE

THREE GUATEMALAN VILLAGES, 1958-62

Age (Years)	No. of Children	Shigella		Salmonella		Escherichia coli (EPEC)	
		Carriers	%	Carriers	%	Carriers	%
1	647	10	1.5	1	0.2	31	4.8
1	690	61	8.8	0	-	38	5.5
2	678	71	10.5	1	0.1	25	3.7
3	676	69	10.2	0	-	24	3.6
4	459	35	7.6	2	0.4	14	3.0
Total	3,150	246	7.8	4	0.1	132	4.2

Source: Acute Diarrheal Disease in Less Developed Countries.
Gordon, J.E., Behar, M., Scrimshaw, N.S., Bull WHO, 1964.

Table 3

DEATHS FROM ACUTE DIARRHEAL DISEASE BY AGE

THREE GUATEMALAN VILLAGES, 1950-59

(Years)	Deaths from Acute Disease	Death Rate*	Deaths as % of All Deaths
1	87	16.98	14
1	123	35.63	41
2	102	27.97	53
3	44	12.17	43
4	34	9.63	55
1- 4	303	21.27	46
5-14	70	2.55	41
15+	117	1.95	16
All Ages	577	5.42	27

*Rates are per 1,000 population.

Source: Acute Diarrheal Disease in Less Developed Countries.
Gordon, J.E., Behar, M., Scrimshaw, N.S., Bull WHO, 1964.

clinical illness is not sufficiently distinctive. Laboratory study is very expensive.

Typhoid. Salmonella typhi, the cause of typhoid fever, is spread from humans usually via an intermediary vehicle--often food--to other humans without animal involvement. S. typhi is rarely transmitted person to person. The infection occurs throughout the world, and its prevalence is used as a measure of inadequate public health control of food and/or water distribution. For most individuals, the dose necessary to initiate an infection is high so that even when an infected person resides in the household, the infection is rarely passed directly from one person to another. In endemic areas, the disease is often diagnosed correctly without laboratory tests on the basis of clinical symptoms. Antibiotics, usually chloramphenicol or ampicillin, are used in treatment; most strains remain sensitive to these antibiotics. Outbreaks of typhoid, however, have occurred in which the causative organisms were found to be resistant to chloramphenicol or ampicillin. In areas where typhoid is endemic, the most frequently involved groups are school age children: the disease also demonstrates a seasonal pattern associated with water scarcity and periods immediately before and after onset of the rainy season. Excretion of S. typhi is occasionally prolonged (carrier state), especially in women over 35. The carrier state is very infrequent in children. Since carriers are often found among women, often those who handle foods, the possibility exists for transmission of S. typhi in commercially or home-prepared foods. A moderately effective vaccine against typhoid is available, but the groups at greatest risk of disease are precisely those most difficult to reach by immunization. General immunization does not appear to be a cost effective control procedure. Laboratory tests are available to diagnose typhoid serologically, but the tests require paired sera and are rarely used correctly.

Salmonella Other Than S. Typhi. Salmonellae commonly infect animals: infections in humans are ordinarily related to contacts with animal products or contamination of foods or water in environments themselves contaminated by Salmonella from animal products. In developed countries, reported infections occur most frequently in children under one year and preschoolers. Illnesses among infants are often the result of other infections associated with foods which occur in the home. In developing countries, dissemination of Salmonella infections in hospital patients is a common problem: transmission in the community associated with foods must also be common, but it is less frequently described. Lack of such reports is probably related to absence of study rather than absence of infection.

Salmonellosis is an acute febrile illness whose symptoms most often include nausea, vomiting, abdominal pain, and diarrhea. The disease is often treated with antibiotics, although such treatment is generally unnecessary and ineffective. Salmonellae are frequently resistant to antibiotics. The dose needed to initiate an infection is usually high, and person-to-person spread uncommon. Foods are the common vehicle. Salmonellae are often found in commercial products which include meats, poultry, eggs and egg products, chocolate, and powdered milk among others. As a result salmonellae often cause disease in populations that use commercially prepared foods which have been inadequately refrigerated. There are no effective vaccines for Salmonella (except typhoid). Diagnosis requires the isolation and identification of the organism. Serologic tests are not routine or specific.

Cholera. Vibrio Cholerae, the cause of cholera, is spread from humans to other humans via an intermediary vehicle, often water or water-contaminated food. Cholera is rarely transmitted directly from person to person, probably because of the large dose needed to initiate an infection. Since it is an internationally quarantinable disease, there are, in addition to the medical problems, political overtones in the reporting and subsequent handling of this disease. Since 1961, the major cause of clinical cholera in the world has been Vibrio Cholerae biotype El Tor. This strain of cholera is characterized by frequent occurrence of symptomless infections. As a result, quarantine measures are essentially ineffective since many infected individuals are not seriously ill and would not be picked up by control measures aimed at clinically ill persons.

In endemic areas, the most frequently involved group is preschool children. Outbreaks often start in adults, and subsequent transmission depends on the vehicle of transmission and the mode of spread. If food is the vehicle, then spread depends on who most frequently eats that food. If contaminated water is the vehicle, essentially everyone who drinks the water will be at risk. Persistent carriers of Vibrio Cholera are infrequently found.

Cholera vaccine has a long but disappointing history. The vaccine is relatively effective in preventing disease, but protection lasts for only three to six months. In immunized individuals, infection still may occur but without clinical symptoms. Therefore, immunization does not prevent spread of the infection. Newer vaccines are being developed; but generally, vaccine plays a minor role in the control of cholera.

Treatment of the disease required rapid and massive amounts of oral and/or intravenous fluid therapy, which can be given in field clinics or in the hospital. Tetracycline for five days is effective in eradicating carriage. With early and adequate therapy, deaths in hospitalized patients are less than 1%. Diagnosis can be made clinically in severe cases, but a laboratory is required for diagnosis and/or study of other diarrheal cases and for testing contaminated foods and water.

Other Enteric Bacteria. Staphylococcus aureus, Clostridium perfringens, Vibrio parahaemolyticus, Bacillus cereus, and other enteric bacteria frequently cause outbreaks of enteric disease associated with inadequately refrigerated or prepared foods. The incidence of common source foodborne disease even in developed countries is incompletely known because investigation and laboratory study of foodborne disease outbreaks are infrequent and a substantial proportion of reports filed are inadequate. Existing data in developed countries suggests Staphylococcus, Salmonella, and Clostridium perfringens are the commonest causes of foodborne disease. The illnesses are characterized by various combinations of nausea, vomiting, abdominal pain, fever, and diarrhea which occur predominantly between 2 to 36 hours after a meal. The diseases are generally self-limited. In the

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United States, the commonest reasons for outbreaks due to these agents are inadequate refrigeration before and after cooking, and inadequate handling and preparation in the restaurant.

Evaluation of the Enteric Disease Problem

In the absence of laboratory diagnosis, measurement of enteric diseases in developing countries must rely on counting cases with the clinical syndrome rather than disease due to a particular etiologic agent. For example, deaths due to "diarrhea" are commonly used as a measure of the adequacy of health services, but it is not possible to specify that some portion of these deaths resulted from a specific bacterial, viral, or parasitic agent. A typical description of deaths due to diarrhea is that presented by Gordon et al. for a group of villages in Guatemala (Table 3, page 102). With such data, comparisons of the relative significance of diarrheal disease in selected age groups can be made. However, in most instances, the cause of death indicated to be diarrhea is not determined by a doctor. Furthermore, some deaths, regardless of cause, are not reported. Despite these defects, almost all countries attempt to collect death information by age, data, location, and presumed clinical cause. During epidemics, cemetary records may be useful to gauge the magnitude of a problem if no other system of recording deaths makes such information available rapidly.

A second measure of enteric disease--visits to outpatient clinics--may be obtained in those countries where most outpatient medical care is furnished by the government. Although such visits cannot measure the occurrence of all diarrheal illness, the age and sex of individuals with diarrhea who attend outpatient clinics are usually available for analysis: the records often include month of visit, occasionally village of residence, and whether the residence is an urban or rural area. In some countries, separate tabulations are kept of clinic visits for diarrhea with and without blood in stools. Stool cultures are occasionally obtained in hospital outpatient clinics. It is not unusual to find a tabulation of outpatient visits for the preceding year, although these tabulations are occasionally several years late in publication. If clinic visits for diarrhea are known as well, then the frequency of diarrheal visits per 100 clinic visits can be calculated and used rather than the simple frequency of diarrheal visits per month. Diarrheal visits per 100 visits are most useful if they are tabulated separately for the preschool group since that is the group with the most frequent and severe diarrheal illness.

Admissions to hospital wards can be used as another measure of enteric disease incidence. In hospitals, laboratory data resulting from stool or blood cultures are occasionally available, although they relate only to the most seriously ill children. Since most hospitals are urban, hospital admissions may not represent the age, sex, and seasonal characteristics of serious diarrhea in rural areas.

In developed countries, laboratory-based enteric disease surveillance is common. In those countries where specific etiologic agents are identified by stool culture, the characteristics of the agents and the persons from whom they are obtained may be tabulated rather than the simple frequency of clinical illness.

In these countries also, annual data provide frequencies of Salmonella and Shigella by serotype and some data about E. coli, campylobacter, vibrios, and other agents. The data often are presented by season, age, and geographic area.

In developing countries, the use of laboratory tests is infrequent; the patients studied (often urban rather than rural) are unlikely to be representative of the population or their problems, and the available laboratory data are so incomplete that they are rarely utilized. However, even in developing countries, analysis of culture results is helpful since the data give a crude picture of the spectrum of bacteria associated with disease and suggest whether changes in bacterial resistance to antibiotics have taken place. In addition, the laboratory can identify agents new to a particular population, such as Shigella dysenterii type 1, which occurred in epidemic form in Central America in the late 1960's; or Salmonella typhi resistance to ampicillin when it occurred in an outbreak in Mexico. Salmonella serotyping, occasionally performed in major reference laboratories, is a basic step in indicating common source foodborne outbreaks. Identification of Vibrio cholerae, in cases of severe diarrhea, is essential in confirming the etiology and in the control of a cholera outbreak.

The laboratory is a key component of disease investigation and support for the study and control of enteric disease. The problem in developing countries is to develop coordination of field study with the laboratory. Investigation of enteric disease outbreaks is the most efficient way to utilize laboratory and field services. If appropriately done, such investigations pinpoint the specific etiologic agent and mode of spread. Appropriate actions taken when that information is known may lead to control of a problem not only in the specific instance but throughout an area. Investigations of enteric disease are most frequently undertaken for typhoid fever, but similar actions are equally appropriate for any common source foodborne or waterborne outbreak.

The work of epidemiologists in developing countries is often limited to tabulating disease data and printing weekly, monthly, and annual reports. Since investigation of enteric disease outbreaks is perhaps the most important way to understand the epidemiology and control of enteric disease, it is important that efforts be made to support and amplify the activity of the national epidemiologist and the enteric bacteriology laboratory so that outbreaks can be investigated thoroughly.

Developing Programs to Reduce Mortality and Morbidity

In setting priorities for enteric disease programs, first place must be assigned to short term efforts to reduce mortality. As indicated, many different bacteria cause diarrhea in children. The clinical picture varies with the etiologic agent, but the treatment in almost all instances is focused primarily on rehydration. As a result, efforts at reducing mortality depend less on the infectious agent that they do on prompt and appropriate delivery of medical services.

Recent studies have indicated that delivery of oral therapy to children with acute enteric disease is effective, inexpensive, and can reduce mortality significantly. In outbreaks of cholera in rural areas in Bangladesh, for example, where the case fatality of untreated cholera cases can be as high as 50%, rapid delivery of oral rehydration reduced death to less than ½ of 1%.

Programs to be developed should focus on delivery of rapid rehydration at the local level. Programs to achieve this objective can be evaluated through use of existing surveillance information or information gathered by the treatment program.

Reliable and complete death data are needed to measure effectiveness of an oral treatment program in rural areas of developing countries. Therefore, efforts should be made to improve the reporting of deaths and the underlying cause given on death certificates, particularly if it is diarrhea. Regardless of the size of the area chosen for particular emphasis, death reporting systems can be evaluated for completeness and accuracy. When death reporting systems have been improved so they are reasonably complete, the information about age, season, and cause of death can be utilized to evaluate efforts made to reduce mortality. Protocols appropriate for the introduction of oral fluid therapy and its rapid and inexpensive delivery in rural areas have been developed and described by WHO, PAHO, and centers for diarrhea research. The educational component of the delivery of health services is an integral part of the control effort. Early case finding and rapid utilization of available facilities are needed if the effort to reduce mortality is to be effective.

Any program to reduce morbidity, an intermediate objective, requires careful focusing of the limited resources available. Control programs should begin with attempts to understand the magnitude and character of the enteric disease problem through utilization of available surveillance data. An improved surveillance system should lead to the ability to locate problem areas and to identify in those areas the source of the problem amenable to control. Although the populations of most developing countries are predominantly rural, the urban population is growing: the problems of urban crowding and poverty are occasionally even worse than in rural areas. The hospitals, usually located in urban areas, are often better measures of urban than rural problems.

The enteric disease laboratory is usually the weakest link in the chain of efforts made to understand and then control enteric disease. It is usually hospital based, inadequately staffed and supervised, poorly funded, overworked, and therefore, plays little role in any control effort. Even the national laboratory, which might function as a reference center, often fails in this function and is little more than an adjunct to a hospital. Part of this disappointing story is understandable since most patients with diarrhea are treated symptomatically despite the laboratory result. Often the diarrheal illness is viral in etiology, and these illnesses can be managed only symptomatically with fluids. Finally, physicians often do not trust the laboratory result. Distrust is based on experiences with frequently questionable results received often after excessive delays. To break this cycle, it is necessary to improve the quality of the laboratory and then to maximize the use of the laboratory in ways that lead to control of enteric disease.

One effective way is as a monitor of the occurrences of new epidemic problems, such as cholera. What is required is that studies of enteric disease outbreaks get first priority for laboratory study and that the laboratory study be coordinated by a central reference laboratory. The reference laboratory should be both a reference center for all hospitals and clinics and the laboratory which performs tests in the study of outbreaks.

Conclusions, Comments, and Recommendations

In planning programs to reduce the magnitude of enteric disease in developing countries, it should be abundantly clear that major reductions will result from improved water supplies, raised socioeconomic status, reductions in number of children per family, and longer intervals between births. Better sanitary and economic conditions will effect a reduction in the magnitude and character of the enteric disease problem without any efforts devoted either to medical care or to specific disease problems. In the developed countries, the major decreases in enteric disease morbidity and mortality occurred before modern therapy was available, before improvements in medical care, and before the availability of health care in general.

Major efforts are being made in many developing countries to improve water supplies and waste disposal systems. Concurrently, programs are being carried out to promote family planning, health education, and to improve the delivery of medical care. Thus, it will be virtually impossible to separate the specific effect and the relative cost benefit of any one of these components from the total. Regardless of the difficulties in measuring costs versus benefits, it does appear that general improvements in water supply, education, and reductions in number of preschool children in the family all lead to some reduction in enteric disease magnitude.

Mortality reduction clearly deserves first priority in enteric disease control programs. Programs to reduce mortality have been designed by WHO and are being tested in many countries. They include demonstration projects supervised by medical school personnel which attempt to show that oral rehydration is an effective therapy in severely ill children. Subsequent demonstration projects in outpatient clinics which utilize the same oral rehydration program, attempt to reach children before they are so severely ill that they must be brought to the hospital. Finally, some programs demonstrate the use of oral rehydration on children before they reach outpatient clinics as a way of reducing the frequency of severe life-threatening diarrhea.

In order to establish that reduction in mortality has been achieved by the control program, it is necessary to select an indicator area. Such an area, department, district, or division which has several clinics and a known population can be studied to determine how often deaths occur in children and how adequately the causes of death are recorded. These data which are continuously collected can then be used as indicators when an oral rehydration program is initiated.

Programs to study diarrheal deaths can be integrated with an enteric disease laboratory study of the etiology of diarrhea, if such a study is in progress. Demonstration programs might begin with hospitalized cases and then be expanded to include limited studies of outpatient diarrhea. In this way, the study of deaths due to specific etiologic agents can become a part of the program to limit diarrheal deaths in children.

Reduction in diarrheal morbidity should get second priority. Programs to achieve such reduction are outpatient oriented and presume that attempts to eliminate contaminants in water, food, etc., may significantly reduce diarrheal morbidity. Since many of the agents that cause diarrhea are transmitted from person to person and since hygiene in preschool children is lax, it is likely that only a moderate reduction in diarrheal incidence can be achieved by decreases in environmental contamination and the provision of water for personal hygiene.

Any attempt to demonstrate a decrease in outpatient diarrheal visits also requires the selection of indicator areas as well as the analysis of a clinic visit data by age, resistance, etc. Since baseline incidence data are necessary to show a decrease has been achieved, collection of information can begin without the laboratory and without money for improvements in water and sanitation. If the indicator area is sufficiently large and diverse, it may be possible to study the frequency of diarrhea in areas with and without water, as well as the character and frequency of diarrhea in areas before and after water and sanitary facilities are made available. Integration of the laboratory into studies of outpatient diarrhea is difficult but might be attempted by studying the changing frequency of Shigella, an agent commonly transmitted person to person, as a measure of the efficacy of the control method(s) being evaluated.

A third priority in the control of enteric disease is the investigation of outbreaks. As has been mentioned earlier, outbreak investigation leads to an integrated use of laboratory and epidemiologic services and also can lead to elucidation of the mode of spread of a particular agent in the community--information necessary for control. In addition, investigation of outbreaks focuses laboratory facilities on a particular problem. This is preferable to restricting the laboratory to studies of clinical material where the results do not often lead to specific changes in therapy.

This paper has emphasized that enteric disease control requires laboratory support: the most efficient and effective utilization of the laboratory is in studies designed with an epidemiologic purpose. Since the government often has little control of medical school laboratories and hospital laboratories are devoted primarily to studies of clinical illness, effective control of enteric diseases requires the development of a government directed enteric disease laboratory which would be available to work with national epidemiologists in studies of outbreaks and evaluation of enteric disease control efforts.

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PARASITIC ENTERIC DISEASES

by

Frederick L. Dunn

Enteric parasitic diseases are found throughout the world, but they occur with greater frequency in the developing countries. Warm climate and the relatively less well developed personal and environmental sanitary conditions in developing countries are the main factors which account for this difference in prevalence.

Because of their size, the large parasitic worms were among the first agents noticed and studied as probable causes of human disease. Adults in most traditional societies today recognize the worms of several species to be agents of intestinal disorder; ancient peoples presumably did so as well. Modern parasitology dates from 1379 when Jehan de Brie discovered the liver fluke, Fasciola hepatica, in sheep; but progress was slow until the compound microscope was developed in the 19th century.

Control of enteric parasites in developing countries has not yet been possible because of the multiplicity of agents involved and the general lack of preventive measures other than improvements in environmental sanitation. This paper presents an overview of these parasitic diseases and the public health problem that they represent in developing countries.

Many protozoa and helminths which infect the human gastrointestinal tract are parasites whose distribution is cosmopolitan.

Of 16 species of enteric protozoa identified in man, only five are recognized to be consistently pathogenic. Of these, only three species--Entamoeba histolytica, Giardia lamblia, and Balantidium coli--occur with any frequency in human populations. E. histolytica and G lamblia are truly cosmopolitan parasites; in many countries, amebiasis and giardiasis constitute public health problems, either as endemic diseases of high prevalence or because of sporadic disease outbreaks.

Among helminths associated with the gastrointestinal tract at some stage in the parasitic life cycle, at least 20 species must be regarded as important to man because of high prevalance and/or potential pathogenicity. Severity of disease is usually related to intensity of infection, that is worm burden. These species include seven trematodes or flukes, five cestodes or tapeworms, and eight nematodes or roundworms. The species numbers could easily be doubled if helminths reported from man only sporadically were to be counted.

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The principal cestode (tapeworm) parasites of man are: the fish tapeworm, Diphyllobothrium latum; the hydatid worms, which cause echinococcosis, Echinococcus granulosus and E. multilocularis; the port tapeworm, Taenia solium; and the beef tapeworm, Taenia saginata.

The most important trematodes (flukes) associated at some stage(s) with the human intestinal tract are: two of the three principal human schistosomes, Schistosoma mansoni and S. japonicum; the liver fluke, Clonorchis sinensis; the sheep liver fluke, Fasciola hepatica; the giant intestinal fluke, Fasciolopsis buski; the Opisthorchis liver Flukes, O. felineus O. viverrini; and the lung fluke, Paragonimus westermani. Some might argue that several other flukes, e.g., Heterophyes heterophyes, Metaconimus yokogawai, should be added to this list because of their local significance in some countries.

Eight important nematodes (roundworms) are parasitic in the gastrointestinal tract during some stage(s) of their life cycles. Two of these species--Dracunculus medinensis (the Guinea worm) and Trichinella spiralis (the agent of trichinosis)--are not really "enteric" parasites; their modes of transmission require ingestion of infected Cyclops and uncooked pork, respectively; but the intestinal stage of infection is transient and of little or no clinical significance. The other parasites are truly enteric: Ascaris lumbricoides, the common roundworm; Enterobius vermicularis, the pinworm; the hookworms, Necator americanus and Ancylostoma duodenale; the threadworm, Strongyloides stercoralis; and the whipworm, Trichuris trichiura.

Some of the helminths listed above are extremely common in many human populations, particularly those in which poverty is widespread. Nearly universal prevalence is not unusual for Ascaris, Trichuris, and the hookworms in some populations in tropical and subtropical developing countries. In 1947, Stoll published estimates of human infection with most of these helminths for the entire world.[10] He concluded that about 30 percent of the world's population, or 644 million persons, harbored Ascaris at that time. For hookworms, he estimated 457 million infections; for whipworms, 355 million; for pinworm 209 million; and for Guinea worm, 48 million. These numbers, calculated when the world population stood at about 2,200 million, would probably be doubled today. Little has happened in the past 30 years to alter the circumstances of transmission for most enteric parasites in those sectors of the developing world where the parasites were especially prevalent and where populations have now more than doubled.

It was stated above that poverty is associated with high prevalence of enteric helminth infection. This holds true as well for the intestinal protozoa, both the pathogens and the commensals. Although other factors discussed below are also important in transmission, it is inadequate sanitation, in the broadest sense and its association with poverty, that governs the level of enteric parasitic infection in a community. A World Health Organization committee commenting on the public health importance of helminths summed up these interactions succinctly:

"Helminthic infections as a whole can be viewed as providing, by their prevalence, an index of a community's progress towards a desirable level of sanitation. Successful management of pollution problems will eliminate essentially all of the helminths except those of the arthropod-transmitted group, and the elimination of mosquitoes and other arthropod pests will, of course, control the arthropod-transmitted helminths as well. Thus, to whatever extent a community falls short of having attained living standards based on these desirable conditions, helminths will have important bearing on the people's health. It is also true, of course, that high standards of living depend on high levels of physical vigour and health. Thus, the helminths are important to whatever extent they detract from the vigour of the community."[12]

The same WHO committee classified modes of helminth transmission into five groups:

> Contagious or fecal-borne transmission. Eggs or larvae are infective when passed (or when deposited at the anus by the pinworm). Direct person-to-person transmission can occur.
>
> Soil transmission. Eggs or larvae become infective after a period of incubation in the soil. Ascaris, Trichuris, and the hookworms belong to this important transmission group.
>
> Arthropod transmission. Infective stages develop in arthropod intermediate hosts which transmit the infection when biting or when ingested by man. The Guinea worm is the only representative of this transmission group among the important enteric helminths.
>
> Snail transmission. Infective stages develop in snail intermediate hosts or in second intermediate hosts after partial development in the snail. The schistosomes and several other flukes are transmitted in this fashion.
>
> Food animal transmission. Infective stages develop in animals whose flesh is an item of food for man. Into this group fall Trichinella, most of the tapeworms, and several of the intestinal flukes (whose modes of transmission actually represent combinations of groups 4 and 5.)

Intestinal protozoa are transmitted by the contagious of fecal-borne route directly--by ingestion of raw vegetables, by ingestion of water, through contamination caused by flies and perhaps other insects, or through the actions of food handlers.

Another approach to classification of the enteric parasites sorts them in relation to temperature dependence and geographical distribution. Temperature-dependent parasites have definite maximal and minimal temperature requirements during those stages in the life cycle that occur outside their hosts. Such parasites are usually geographically limited, transmitted throughout the year in the tropics and more or less seasonally in the subtropics. The intentinal trematodes, the soil-transmitted hematodes, and the Guinea worm belong to this group.

Temperature-independent parasites are potentially transmissable everywhere and are not restricted grographically by environmental temperatures or other climatic factors. Parasites in this category which do not have a cosmopolitan distribution are localized because of sociocultural and behavioral determinants (including control measures) rather than physical environmental constraints. Contagious or fecal-borne parasites are temperature-independent and potentially cosmopolitan. Many food animal transmitted parasites are also temperature-independent but tend to be geographically restricted by cultural factors, e.g., subsistance practices.

Surveys have demonstrated the profound influence of human behavior on transmission of enteric parasites. Striking differences in parasite prevalance and intensity of infection occur in human populations not only in relation to age and sex but to socioeconomic status, religion, sanitary practices, house styles, and a long list of other social, cultural, and behavioral variables.[6, 8, 11] Understanding of the public health problem presented by enteric parasites in a community depends upon parasitological survey data, studies of the physical environment (e.g., soil characteristics), and epidemiologic and ethnographic studies of human behavior and its determinants.

The most important enteric protozoan diseases are amebiasis and giardiasis, but balantidiasis is locally important in a few tropical areas, especially in Melanesia. All three of these infections require treatment on recognition when symptoms are present. However, asymptomatic Giardia infections (cysts in the stools) are often left untreated in developing countries.

Chronic, recurrent diarrhea, alternating with constipation, is the usual manifestation of infection with Balantidium coli, but attacks of dysentery may occur intermittently; severe infections may be fatal. Giardia infection may cause acute or chronic diarrhea, cramping, distension, tenderness, and other troublesome abdominal symptoms. Infection with Entamoeba histolytica usually becomes manifest as diarrhea or dysentery with abdominal cramps or because of tenderness and enlargement of the liver. The most common complication of intestinal amebic infection is liver abcess, but the parasites may travel to other sites also. Bowel perforation occurs occasionally. Mortality in untreated amebiasis may be high, but the prognosis with modern chemotherapy is very favorable.

All of the enteric helminths noted earlier are capable of causing clinical signs and symptoms, usually abdominal, but the severity and persistence of these manifestations are normally related to worm burden. In the case of hookworm infection, for example, severity of anemia is clearly related to intensity of infection. Two or more species often coexist, e.g., the intestinal nematodes Ascaris, Trichuris, and hookworm; symptoms will be a product of the combined effects of these parasites in their host. Fatalities due to enteric helminths are unusual when worm burdens are light. However, death may occur in chronic, heavy infection by several helminth species, particularly when associated with malnutrition and concurrent infection by other infectious agents. Adult tapeworms (D latum, T. solium, T. saginata) often occur singly; these parasites become increasingly troublesome as they increase in length, compete for more nutrients, and occupy more space in the intestinal lumen.

Treatment of enteric helminthiases depends, in general, upon the presence or absence of symptoms. Light and clinically inapparent infections are often left untreated in endemic areas where rapid reinfection is probable. When symptoms occur, treatment is indicated to reduce the worm burden or to eliminate the parasites, at least temporarily.

Assessment of Enteric Parasitism in the Community

Surveillance methods developed for acute communicable diseases are seldom appropriate for monitoring enteric parasites in developing countries. Most enteric parasitic disease is chronic, asymptomatic infections are frequent, and the prevalence of infection (and disease) is often high. Where prevalence is high, control programs are usually nonexistant so surveillance, per se, serves no useful purpose. In areas where enteric parasites occur rarely or only sporadically, however, a communicable disease surveillance system may provide an early indication of an outbreak of one of the several diseases--e.g., amebiasis, giardiasis, trichinosis--which can occur in epidemic fashion.[4] Hospital and clinic records are of little value in assessing the extent of enteric parasitism in the community, especially in developing countries. These records serve only to indicate which species are certainly present in a population.

For most of the enteric parasites, the basic diagnostic procedure is the examination of one or more stool specimens for cysts, trophozoites, eggs, and larval or adult worms (or cestode segments). Other diagnostic methods are usually only supplementary. In the diagnosis of amebiasis, for example, a search for trophozoites and cysts in stool specimens is the procedure of choice while serologic tests, aspiration of liver abscesses, and endoscopy are of secondary importance in most cases. In trichinosis, on the other hand, skin testing and detection of eosinophilia are essential for diagnosis.

Under clinical conditions, it may be necessary to examine a series of stool specimens to confirm the presence of a parasitic infection. In assessing parasitism in a community, however, modern survey methods have made it possible to limit studies to single stool specimens obtained from a sample of individuals in the population. Any enteric parasite survey--regardless of the diagnostic procedure employed--should provide not only prevalence data for protozoa and helminths in the population; but also, through egg-counting, some indication of the intensity of the helminth infections. For many years, direct smear egg-counting has been employed for routine field surveys. Such smears can be prepared either from fresh stools or from preserved stool material, e.g., in MIF (TIF).[2,5] Several concentration methods have also been devised to increase sensitivity for detection of very light infections.[3] When greater sensitivity is required than that provided by examination of pairs or multiple of direct smears, the Kato thick-smear technique is now the method of choice for survey work.[7,9] The references cited above will introduce the reader to the very extensive literature on this subject.

Control: Ascariasis

Because of the great diversity of agents, modes of transmission, and epidemiological patterns, it will not be feasible to discuss control of enteric parasites except at a general level. In anticipation of this discussion, however, it may be useful to take note of the approaches to control that have been employed in a single case, that of ascariasis, the most prevalent of all helminthiases. These approaches are reviewed in a World Health Organization committee report, Control of Ascariasis.[13] Although published a decade ago, this report is in no important respect outdated. Research on ascariasis and its control continues to advance very slowly.

The 1967 report emphasizes four elements in the control of ascariasis: basic biological research, epidemiological research and surveys, specific approaches to control, and organizational considerations. In order to determine whether control should even be considered, it is necessary to establish the level of endemicity of ascariasis in the region, country, or locality. This depends upon determination of the prevalence and intensity of human infection. Also needed are estimates of the number and distribution of viable and infective eggs in the soil (or in each of several soil types) in the area. These subjects are fully reviewed in the WHO report and its methodological appendices.

Surveys required for assessment of endemicity will normally also provide information on the status of other enteric parasites in the same areas. It may be decided that some effort should be directed toward one or more of these agents at the same time that control of Ascaris is initiated. The objective of these studies should be to provide a true measure of the magnitude of the public health problem presented by these parasites. No commitment of funds, equipment, and personnel for control is justified without these baseline data.

If a decision is taken to proceed with control of ascariasis, the currently recognized approaches are three: mass chemotherapy, environmental measures, and health education (based on adequate behavioral research). The 1967 report notes that chemotherapy employed in control must be clearly distinguished from radical cure of the individual patient.[13] In most control programs, eradication of the parasite is not the aim; radical cure of everyone in the community is not a realistic goal. (The eradication concept has, however, been applied with considerable success in Japan where mass chemotherapy programs were combined with other control measures.)

Maintenance of control depends upon appropriate modifications of human behavior. These are usually effected by programs in health education in conjunction with environmental measures which for ascariasis comprise at a minimum: "...the safe disposal of human excreta; the provision of adequate and safe water supplies in such a way as to promote a higher standard of personal hygiene in the population; and the prevention of food contamination by faecal material."[13]

The report also notes that additional environmental measures should: "deal with the improvement of housing and housing hygiene and with general community development", and it stresses two points: "(1) To be truly effective, environmental sanitation measures require the understanding, support and active participation of the people concerned. Mere technical improvement of the environment is insufficient without general education in hygiene and sanitation. (2) Health administrations should take the initiative in stimulating such participation and in providing essential technical guidance. Venezuela's successful rural sanitation and rural housing programmes are examples of what can be done."

Control programs in Japan which combine mass chemotherapy, environmental approaches, and public education in personal hygiene have proven effective in eliminating ascariasis from large areas of the country. The organizational aspects of such a campaign are described in detail in the 1967 report.[13] A successful program rests on a long-term commitment and regular evaluative studies. However, such programs are costly in resources and may be less feasible in the tropical and subtropical zones where ascariasis is often hyperendemic. It must also be noted that in countries outside the tropics, e.g., in Europe and North America, the prevalance of ascariasis has fallen sharply in recent decades as an unplanned by-product of improved living standards and general acceptance of relatively high standards of personal hygiene.[13]

Control: A General Comment

The elements of an ascariasis control program are also the essentials in the control of most of the other enteric parasites. For some of the other species, assessment may depend upon other methods--e.g., skin testing, sputum examinations, serological tests--but the basic elements of the control program remain the same. Those elements are: mass chemotherapy, environmental measures to improve sanitation, the health education to enhance personal and public hygiene. The WHO report on ascariasis is recommended as a review of principles that have broad applicability. Immunization procedures have almost no role in the control of these parasites and require no comment here. Control of intermediate hosts or of infection in reservoir hosts, however, may be a major element in programs of control for enteric parasites in the arthropod, snail, and food animal-transmitted groups. These alternative hosts complicate local epidemiological patterns but also provide opportunities for interruption of transmission that do not exist in the contagious and soil-transmitted categories. It is increasingly clear, however, that control programs focused solely on snails, for example, are not likely to prove any more successful in the long term that programs for other parasites based entirely on mass chemotherapy or on latrine construction.

All experience to date indicates that, except in very special cases, enteric parasite control must rest upon combined approaches as outlined above for ascariasis. Such programs should preferably be directed toward simultaneous control of all enteric parasites of public health importance in a locality or region. This approach may be feasible--and the resources to attempt it may be available--in the most prosperous countries. Unfortunately in the rest of the world, deliberate large-scale programs of enteric parasite control are probably out of the question in current circumstances. In most endemic areas where control has been attempted, mass reinfection has soon occurred.[1] It is difficult to justify expenditures of public health funds on such programs or on extensive community surveys which cannot be followed by effective control programs. In these circumstances, a selective approach to enteric parasitism is the best option; that is, treatment of those who are symptomatic and of those who, while symptom-fee, carry the heaviest worm burdens.

These parasitic diseases will probably recede in importance only gradually as a consequence of evolutionary changes in general well-being, education, and economic conditions which may follow new movements toward greater social justice.

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TRACHOMA

by

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Trachoma, a chronic inflammation of the mucous membranes lining the eyelid and eyeball, is still the leading cause of preventable blindness in the world today. The disease is endemic in ruralpopulations of less developed countries, particularly in drier tropical and subtropical regions. Blinding trachoma is a major public health problem in North Africa and sub-Saharan Africa, in the Middle East, in the drier regions of the Indian subcontinent, and in Southeast Asia. In addition, pockets of blindness trachoma exist in Australasia, the Pacific Islands, and Latin America. The disease has always been more prevalent in poorer populations; when the benefits of economic development reach trachomatous populations, the disease becomes milder and sometimes disappears entirely.

The etiologic agents of trachoma and inclusion conjunctivitis (TRIC agents) were originally believed to be viruses but are now classified as Chlamydozoa. Trachoma results from infection of the conjunctive with Chlamydia trachomatis serotypes A, B, Ba, and C. In hyperendemic regions where the disease causes blindness, associated bacterial infections (commonly Haemophilus sp. and pneumococcus, rarely epidemic Neisseria gonorrhoeae) contribute to the intensity of inflammation and eventually to the degree of conjunctival and corneal scarring.

In the active, infectious stage, trachoma is typically a chronic conjunctivitis accompanied by numerous lymphoid germinal centers (follicles) visible on the conjunctival surface. This is true especially on the upper tarsal conjunctive which has both follicles and varying degrees of papillary hypertrophy (inflammatory infiltration). Conjunctival follicles appear as elevated avascular lesions that may be yellowish to grey-white, or translucent. They vary in size from 0.2 to 2 mm in diameter. Histologically, they consist of lymphoid germinal centers. As trachoma progresses, the conjunctiva shows fine linear scars in mild cases and broader confluent scars in more severe cases. Tear deficiency syndrome and stenosis of the lacrimal (outflow) duct may be late complications in patients with severe scarring. The major, potentially blinding complications, however, are distortion of the lids, particularly the upper lid, and trichiasis or entropion, the misdirection of the lashes so that they grow at an angle directed toward the eyeball itself. The constant abrasion of the cornea

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by the wirelike lashes and occasional foreign body injuries in a relatively dry eye frequently result in corneal ulceration, followed by scarring and loss of vision.

During active trachoma, there is inflammation of the cornea manifested by discrete infiltrates and rarely by ulceration. In addition to the specific trachomatous involvement of the cornea, there is a high incidence of other corneal disease in trachomatous populations. Superficial scars associated with corneal vascularization are very common. Avascular pearl-like excrescences, called Salzman's nodular dystrophy, may form on the corneal surface. Corneal scarring, which may follow bacterial ulcers of the cornea initiated by trichiasis and entropion or by foreign body injuries, is not infrequent.

The diagnosis of trachoma, according to the Third Expert Committee of the World Health Organization,[1] can be made if two of the following signs are present: lymphoid follicles on the upper tarsal conjunctive; typical conjunctival scarring; vascular pannus; and/or limbal follicles or their sequelae, Herbert's pits.

The presence of at least two of these should be regarded as the minimal criteria for the clinical diagnosis of disease. To establish that trachoma is endemic in a population, these minimal signs should be demonstrated in a significant proportion of suspected cases examined in a community. There are a number of other conditions that closely resemble trachoma; but, with minor exceptions, they are never endemic in a community.

Classification of Trachoma

Trachoma cases are usually classified by "stages" according to the MacCallan classification.[2] Although corneal signs must be present to make a diagnosis of trachoma, the MacCallan classification is based on findings in the conjunctiva alone.[1]

Stage 0: No signs of trachoma.

Stage I: Immature follicles present on the upper tarsal plate, including the central area, but no conjunctival scarring.

Stage IIA: Mature follicles present on the upper tarsus and moderate papillary hypertrophy, no conjunctival scarring.

Stage IIB: Marked papillary hypertrophy of the upper tarsus obscures the tarsal follicles, no conjunctival scarring.

Stage III: Follicles are present on the tarsus, definite scarring of the conjunctiva.

Stage IV: No follicles present on the tarsal plate, definite scarring of the conjunctiva.

"Mature" follicles are defined as "soft" or "necrotic," liable to rupture under light pressure and leave a conjunctival scar. In the past, the MacCallan classification has been extended to include "trachoma dubium," a term used to indicate cases that lack enough follicular hypertrophy and keratitis to make a definite diagnosis of trachoma. The term "prototrachoma" has been used to indicate cases with no definite signs of trachoma but with laboratory evidence of infection with the chlamydial agent.

The MacCallan classification has been of little use in evaluating the impact of trachoma on a community since it fails to differentiate between varying degrees of inflammation and yields no data on visually disabling lesions. For this reason, it has been necessary to evaluate endemic trachoma in a community on the presence and intensity of inflammatory disease and whether disabling complications exist. Classification of intensity is based on scores for lymphoid follicles (f) and papillary hypertrophy (P) in the conjunctiva of the upper tarsus.[3] There are four categories: severe, moderate, mild, and inactive or insignificant as shown in the table following.

Intensity	Follicle Score (F)	Papillary Hypertrophy Score (P)
Severe	F 1, 2, or 3	P 3
Moderate	F 3	P 2
Mild	F 2 (or F 3 if the follicles are less than 0.5 mm in diameter)	P 1 or 2
Inactive or Insignificant	F 0 or 1	P 1 or 2

The criteria for assigning scores to follicles and papillae have been described in detail by Dawson, Jones, and Darougar[3] and appear in the appendix.

The potentially disabling, irreversible lesions are (1) distortion of the eyelids due to conjunctival scarring and (2) trichiasis/entropion. To emphasize potentially disabling lesions and to provide a more direct indication of the risk, it is useful to record trichiasis/entropion separately from conjunctival scarring.

The disabling lesion is dense central corneal scarring (CC 3) which involves the visual axis.

Blinding trachoma in a population can be recognized by the presence of persons who have lost their vision because of corneal opacity or because of a prevalence of potentially disabling trachomatous lesions, particularly trichiasis/entropion. The irreversible changes probably result from prolonged inflammatory disease of moderate or severe intensity. In communities with blinding trachoma, chlamydial infection is always present even though other ocular bacterial pathogens appear to contribute significantly to the intensity of trachoma and to the lesions that impair vision. Low prevalence of potentially blinding lesions will not lead to a widespread visual loss in a community. This epidemiological situation may be designated as "nonblinding trachoma." Relatively mild cases, uncomplicated by the other ocular pathogens so often found in blinding trachoma, are referred to in the French literature as "trachom pur." From the public health point of view, failure to distinguish blinding from nonblinding trachoma can make it difficult to order priorities and select areas for public health programs.

Trachoma has a worldwide distribution. Blinding trachoma is a major public health problem in the area extending from North and sub-Saharan Africa to the Middle East, and in the drier regions of the Indian subcontinent and Southeast Asia. A scattering of areas with blinding trachoma exists in Australasia, the Pacific Islands, and Latin America. Nonblinding trachoma is present in these areas as well as in most of the drier, subtropical and tropical countries. In North America, the occurrence of trachoma is limited to certain ethnic and cultural groups who continue to have relatively low living standards and among whom trachoma was once endemic. Since World War II, a rising standard of living and active control programs have all but eliminated the disease in those European countries formerly affected. Individuals or families migrating from trachoma-endemic areas to the developed countries of Europe and North America have not acted as reservoirs or reintroduced the disease. Because of better living conditions in the industrialized countries, trachoma is rarely transmitted even to younger family members, and if the disease is acquired, it is mild. However, in persons with healed trachoma, recurrences of active disease may be associated with other factors among which are extreme old age, allergic conjunctivitis, or administration of topical corticosteroids. Persons with recurrent active trachoma do not present a health risk to their families or to the community in industrialized countries or urban environments.

In communities where trachoma is endemic, the highest rate of active infection is in children under 10 years. About 5% of adults also have signs of active disease. Because children constitute such a large proportion of the population in hyperendemic trachoma areas, this active childhood disease represents the primary reservoir in the community. Older children and adults with active disease usually have substantial exposure to infectious younger children.

The intensity of trachoma in any particular child appears to be relatively stable. That is, children with severe trachoma continue to have severe disease on follow-up examinations despite the administration of one or more courses of chemotherapy: mild or inactive disease rarely progresses to the more severe stages. It can be assumed that the intensity of disease in any one individual is a result of microbial pathogens and environmental factors. The major host factor is age and there is no convincing evidence of genetic susceptibility to trachoma.

Children with moderate or severe disease are more likely to develop conjunctival scarring severe enough to distort the eyelids and cause trichiasis or entropion. Severe scarring that occurs in early childhood produces progressive distortion of the eyelids even after the infectious, inflammatory process has subsided, probably because the scars progressively shrink and contract. Corneal vascularization associated with active trachoma rarely extends to the pupil where it would obscure vision. Those individuals with central vascularization and corneal scarring appear to have suffered from another disease process, probably corneal ulceration or injury. While visual loss attributable to trachoma may be found in young adults in affected communities, there are more persons blind due to trachoma in older age groups. Not only is the effect of trichiasis and entropion cumulative, but there is also a natural decrease of tear function with age, so that adults with potentially blinding lesions are subject to tear deficiency with dryness and subsequent breakdown of the corneal epithelium and resultant ulceration.

In less severely affected communities, two patterns may occur. In one, relatively few families may have the severe blinding disease, and although the total reservoir of infectious agent is reduced for the community, the affected families continue to produce individuals who become blind. In the second, (noted in Taiwan by Assaad and his associates) the onset of disease occurs later and the disease itself is progressively milder: it rarely, if ever, leads to visual loss even though a substantial proportion of the population may be affected.[4]

In many areas where trachoma is endemic, seasonal epidemics of purulent bacterial conjunctivitis begin in the spring, reach a peak in the fall months, and decrease precipitously with the onset of cooler weather. These epidemics are most frequently associated with H. aegyptius, but other ocular pathogens contribute to these episodes or purulent conjunctivitis, e.g., pneumococcus, Staphylococcus aureus, Morazella sp., and rarely N. gonorrhoeae. To complicate matters, however, children in such communities who do not have overt conjunctivitis often carry bacterial ocular pathogens in addition to bacteria known not to be pathogenic for the eye, particularly Streptococcus viridans and diphtheroids.[5] Presumably these bacterial ocular pathogens contribute to the intensity of ocular inflammation, but do not enhance the replication of the chlamydial agent. The highest rates of infection with both chlamydia and bacterial pathogens are found in children with trachoma of severe intensity, a lower prevalence in those with moderage intensity, and very little chlamydial agent in those with mild or inactive disease. It is the children with trachoma of severe and moderate intensity who serve as the main reservoir of infection within affected communities.

Flies that cluster on children's eyes and feed on ocular discharges are another factor in the epidemiology of trachoma. In the southeastern and southwestern United States, these are usually Hippelates species (eye gnats) and in North Africa and the Middle East, they are usually the larger Musca species. Jones found that fluorescein-stained ocular discharges are transferred to the eyes of other children in the same family within 15 to 30 minutes.[6] Flies taken from the faces of Egyptian children were found to harbor ocular bacterial pathogens as well as coliform bacilli.[7] It is highly probable that these flies act as passive vectors, transmitting chlamydial and ocular bacterial pathogens from one child to another in an affected community.

Trachoma has long been associated with poverty; economic development with elimination of the disease or reduction of its severity. It is difficult to identify the specific environmental features of greatest importance in transmission of trachoma; but among them, the presence of young children, crowding, and the unavailability of water in the household seem most important. With the presence of flies, these conditions lead to a condition described by Jones as "ocular promiscuity---the indiscriminate mixing of ocular discharges."[5]

Estimate of Current Problem

Little reliable data on the prevalence of trachoma exists in most endemic areas, but the disease is common in many communities that have a high prevalence of blindness. The WHO Statistical

Report, 1971,[8] has incomplete data: A more recent review was presented by Daghfous.[9] One of the problems in determining the significance of trachoma in any community is that, until recently, most surveys only reported the presence of active trachoma or total trachoma. In order to assess the impact of trachoma as a cause of blindness in any community, it is necessary to determine both the prevalence of severe and moderate intensity disease and of potentially blinding lesions--particularly trichiasis/entropion and corneal scarring. In many areas of high endemicity, 10-15% of the population over age 30 may suffer from visual disability due to trachoma. Throughout the Middle East, 4-5% of the population is blind (vision 20/400 or less in the better eye). Children with active trachoma of severe or moderate intensity have a high probability of becoming blind in adulthood. Any control program must focus on these children.

The initial decision to assess trachoma in a country or region is influenced by several factors, among which are: awareness that blinding trachoma existed in the region, a large number of patients who need surgery to correct trichiasis or entropion, or the ocurrence of seasonal outbreaks of purulent conjunctivitis among young children during warmer months of the year. Even when acute trachoma is endemic in rural populations, ophthalmologists who work in urban settings primarily may be unaware of or deny the presence of the disease because prevalence and intensity may be reduced in urban children or children in families with better living conditions.

Initial surveys to determine the prevalence and intensity of active trachoma should concentrate on children under 8 in the poorest rural villages. If most children attend school, the 6- to 8-year-olds (i.e., first- and second-graders) constitute a convenient, readily available sample. In many poorer rural communities, however, only children from families with a little more money attend school and these children may only have mild trachoma if affected at all. Thus, it is preferable to take a household sample of children to determine the extent of active trachoma. A random sample of adults in the same community will reveal if a substantial number have trichiasis, entropion, or corneal scarring. Surveys should also include a determination of visual acuity based on the WHO standards for visual loss--e.g., the proportion of persons surveyed whose visual acuity is 20/70, 20/200, 20/400, and 20,1200, and light perception only.[10] For nonliterate populations, this can be done with Landolt rings or "E" charts.

The size and selection of the sample depend on the purpose of the survey. To determine the extent of trachoma in a region, selection of widely differing areas for inclusion in the survey is of paramount importance. Less effort needs to be made to register and record individual cases. For evaluation of control activities, other sites should be selected and a sample of the population, i.e., family groups, should be followed at intervals after initiation of control to measure the reduction of disease.

A clinician or epidemiologist experienced in the clinical diagnosis of trachoma is necessary if the findings are to be used by public health authorities as the basis for initiating control programs. Most ophthalmologists are not familiar with the diagnostic criteria and clinical scoring method recommended by WHO for trachoma surveys, nor are they familiar with the age groups and geographic locales that should be given priority in such studies. If assessment surveys for trachoma are contemplated, every effort should be made to contact WHO (Prevention of Blindness Programme) or either of the WHO Collaborating Centres for Trachoma. They are locatedat: FI Proctor Foundation, University of California, San Francisco, CA 94143, USA, and c/o B. Jones, Institute of Ophthalmology, Judd Street, WE1H 9QS, London, England.

It has been suggested that photography of the external eye with a suitable clinical camera and later evaluation of the photographs by experts would eliminate the need for a clinician or epidemiologist familiar with trachoma, and so lessen the cost of carrying out surveys. While photographic evaluation may become a valuable adjunct in carefully monitored clinical trials, there is no substitute for direct examination of the patient by an experienced observer.

The selection of clinical signs and criteria for assigning clinical scores as described by Dawson, Jones, and Darougar[3] have now been (unofficially) accepted by WHO. Examinations should be done with binocular microscopes (at least 2X magnification) and a good light source or with a biomicroscope (slit lamp). WHO has standard cards for recording data from trachoma surveys, but other forms may be used as long as the data formats are compatible with those of WHO.

Suitably trained auxiliary personnel can assess communities for active trachoma and disabling lesions. The level of training necessary for mobile surgical teams to correct lid deformities will depend on the particular region; some countries have sufficient ophthalmologists, others use general physicians, and still others are establishing such posts for trained surgical technicians.

Demonstration of chlamydial and bacterial infection of the eyes of affected persons offers substantial support for clinical surveys. Microscopic examination of Giemsa-stained conjunctival smears is still the simplest, cheapest, and most reliable method for assessing the microbiological findings in hyperendemic trachoma.

Microbiologic assistance is often useful in assessing the prevalence of chlamydial infection in the affected population.[11] Although not the most sensitive technique, the Giemsa stain remains a useful procedure for the detection of chlamydial inclusions in conjunctival scrapings. The use of more sophisticated procedures, such as isolation of the agents (preferably in tissue culture), fluorescent antibody techniques, or microimmunofluorescent serology applied to either serum or tears, may provide useful information but often requires laboratory expertise beyond that available in developing countries. The Giemsa stain is probably the easiest and surest technique to teach to personnel in developing countries. It is also the least expensive laboratory procedure since it requires only slides, microscopes, and trained technologists.

Control/Prevention Programs

Whenever possible, trachoma control programs should be incorporated into existing programs for the prevention of blindness. During the surveys, other causes of blindness should be assessed and appropriate preventive or therapeutic measures should be introduced as part of a program to prevent loss of vision. Trachoma control activities thus constitute one component of blindness prevention programs. According to WHO, "Prevention of blindness may be defined as systematic, community-based action to prevent blindness and visual impairment and to relieve remediable blindness."[12] In planning this action, it is essential to recognize three levels of urgency for national action and for international cooperation.

First, identify communities living in conditions that make it scarcely possible for individuals to remain healthy and to preserve vision. Once conditions which underly preventable blindness in a given community are identified, a very high priority should be given to initial intensive multidisciplinary action to control or eradicate the roots of blindness.

Second, identify communities with a large backlog of readily remediable blindness. When these communities are identified, a high priority should be given to initiating intensive action to deliver ophthalmic care locally, such as surgery for a backlog of cataract or entropion.

Third, integrate eye care with primary health care. Primary health care workers should be familiar with eye problems responsible for the occurrence of blindness in their region. In trachomatous communities, such health workers should be able to identify active and healed trachoma, select cases for trichiasis surgery, and be able to identify other vision-threatening diseases of the outer eye.

Ophthalmologists are not necessary for most of the routine program. Public health nurses or school teachers can be trained to administer the topical antibiotics used in mass chemotherapy programs. The tetracyclines have been the drug of choice for many years and erythromycins are acceptable alternatives. However, research is needed to improve methods of drug delivery to the eye.

The primary objective of public health programs for the control of trachoma is the prevention of blindness. This goal implies that control programs should be extended to encompass prevention of blindness from other causes and not be limited to a single disease. The real challenge in trachoma control lies in designing programs to prevent visual loss in rural populations with hyperendemic blinding trachoma. Programs that are developed must lie within the resources of the country and should evolve into a broad community-based effort to deliver eye care in rural areas.

It has been assumed that degree of scar formation in the conjunctive is proportional to the degree and duration of conjunctival inflammation. If the conjunctival scarring is severe enough, the slowly contracting scars produce distortion of the lid so that the lashes turn into abrade the eyeball itself (trichiasis and entropion). In addition, the scarring decreases the production of tears so that the cornea is more susceptible to drying. Thus the constant abrasion of the inturned lashes and minor ocular trauma leads to superficial corneal abrasions. Without adequate tears, such a lesion becomes infected and the resultant bacterial corneal ulcer all too frequently leads to loss of the eye or corneal scarring with visual disability. This sequence of events is a single disease process. Blindness does not result from a random event described as "acute ophthalmia" but as the inevitable result of a disease process that we call "trachoma."

The individuals who enter the pathway leading to visual disability are those whose inflammatory disease is of an intensity and duration sufficient to produce scarring capable of distorting the lid. Milder cases of trachoma rarely, if ever, acquire potentially disabling lesions since the scars are small and occur away from the lid margin.

While trachoma is always associated with chlamydial infection, bacterial pathogens undoubtedly contribute to the intensity of conjunctival inflammation and thus to the severity of the conjunctival scarring. The chlamydial agent and ocular bacterial pathogens are all susceptible to erythromycin, the Tetracyclines, and sulfonamides. Despite controversy about the efficacy of antibiotics in the treatment of trachoma, it is accepted that chemotherapy reduces the inflammation and thus the potentially blinding lesions.

Lid surgery does reduce the risk of corneal complications in trachoma. Patients with a moderate to severe degree of scarring, however, usually have an inadequate flow of tears, so they still have an increased risk of corneal ulceration after minor trauma to the eye. It has been noted that trichiasis usually occurs in adult life (at an average of 33 in one study) so surgical programs have to be maintained for many years after chemotherapy programs reduce the prevalence and intensity of active inflammatory trachoma among children. Nevertheless, surgical programs have an immediate effect in preventing blindness and are well accepted by afflicted communities.

The decline in trachoma with economic growth is well known and probably accounts for disappearance of the disease in industrialized countries prior to the antibiotic era. When the intensity of active trachoma falls below the minimum level necessary to produce disabling scarring, the disease ceases to be a major cause of visual disability. In developing countries, however, economic development is highly localized and is not likely to benefit communities with blinding trachoma for many years. Since each year that passes commits more children to the blinding pathway of trachoma, it is imperative to intervene in the disease process rather than wait for development to take its sometimes leisurely course.

Strategies of Trachoma Control

Like an army in the field, those initiating trachoma campaigns must base their actions on information about the opposing forces. Systematic evaluation is the only way to determine priorities and to monitor the effect of control programs.

One barrier to assessing the seriousness of trachoma has been the lack of an adequate terminology to describe the active inflammatory disease and the disabling sequelae. The simple procedure described above for active inflammatory trachoma and the potentially disabling lesions is readily applicable in field studies. Individuals are classified by intensity of inflammatory disease in their worse eye. Individuals should be classified for disabling lesions according to the status of the better eye, although total disabling lesions should be recorded. These suggestions on clinical scoring of trachoma have been published in the Bulletin of the World Health Organization and are endorsed by the WHO Scientific Group of Virus Diseases.[3] They are presented in the appendix.

Surveys should be used to identify communities with blinding trachoma which, according to Jones, "...can be recognized in a population by the presence of persons with severe grades of intensity of active upper tarsal inflammatory disease leading to the potentially disabling trachomatous lesions, particularly distortion of the eyelids due to severe conjunctival scarring."[5]

Laboratory studies should be an integral part of assessment efforts. The enormous advances in laboratory techniques useful in trachoma studies are described in detail in a recent WHO publication, "Guide to the Laboratory Diagnosis of Trachoma."[11] In our opinion, the simplest and least expensive procedure to support field studies of trachoma is the examination of Giemsa-stained conjunctival smears. Both trachoma inclusions and pathogenic bacteria can be identified, and studies by our group and others show a good correlation of laboratory findings with intensity of inflammatory disease. Giesma-stained smears can provide an independent, nonclinical assessment of active trachoma in terms of chlamydial and bacterial infection and can be utilized to assess the impact of control programs.

Although the sulfonamides, tetracyclines, and erythromycin derivatives are known to be effective in treating active trachoma, there is still considerable controversy about the choice of drug, route of application, and schedule of administration.

The most extensive studies of these problems have been carried out by Reinhards and his associates[13] in Morocco and by Bietti and his colleagues[15] working in Sardinia and Libya. The studies in Morocco established the present widely used "intermittent" treatment with topical tetracyclines. This group also noted that a single four-day course of oral sulfonamides was as effective as a six-month course of intermittent topical chlortetracycline. Biatti found the best results followed combined treatment with oral sulfonamide and topical tetracycline. In a recent study in Iran, a long-acting tetracycline (doxycycline) given once monthly for six months led to a marked reduction in chlamydial infection.[6]

Oral culfonamides are now considered unsuitable for mass treatment because of the very high rate of untoward reactions--more than 5% in American Indians--and topical sulfonamides are relatively ineffective. The tetracyclines are effective when given systemically, but this use must be severely limited in children under 7 years (a prime target group for treatment) and pregnant or nursing mothers. The almost certain emergence of tetracycline-resistant intentinal bacterial pathogens (an important cause of childhood mortality in trachomatous populations) would militate against such use. Topically administered tetracyclines will continue to be the mainstay of trachoma chemotherapy programs, but there is an urgent need for research on better methods of drug delivery, e.g., higher concentrations, more persistent ointment bases, ocular delivery devices, etc. Erythromycin is a suitable alternative to tetracyclines. Since short-term systemic chemotherapy is quite effective when combined with topical applications, a short-term course of systemic antibiotic (erythromycin or doxycycline) might be considered once yearly at the beginning of topical therapy. Erythromycin estolate should be avoided for oral use because it may cause cholestatic hepatitis.

The schedule of drug administration should be closely tied to the particular population segment to be treated. There are compelling reasons to administer antibiotic treatment to the entire population of trachomatous communities with short, repeated applications of topical antibiotics supplemented once or twice yearly with short course of oral therapy. However, this technique has never been satisfactorily evaluated.

The correction of lid deformities will have a more immediate impact on preventing blindness than antibiotic treatment. In areas with a high prevalence of trichiasis, mobile surgical teams are highly effective in carrying out these simple procedures in affected communities. Surgical programs may have to be extended to regions where active trachoma is no longer a problem but where the previously acquired scarring among older groups still causes lid deformities and visual loss.

Accurate case assessment is critical for surgical programs since only communities with a high prevalance of trichiasis/antropion should be visited by mobile surgical teams. Sporadic cases could be better treated by referral to a regional eye hospital. Moreover, there is a constant rate of trichiasis accumulation in the older population so that there must be continued surveillance of high-risk communities.

In school programs, the actual application of antibiotic ointment is frequently carried out by local persons with little, if any, formal training in health problems. The role of such auxiliary personnel should be expanded in several ways.

They could distribute ointment to households. During their visit, they could treat children and instruct mothers or older children on how to treat young children. They could screen for trichiasis. They could be trained to differentiate simple lid and conjunctival infections from corneal ulcers and other acute conditions which should receive immediate, definitive treatment in an eye hospital.

Training for village health workers should be short, simple and carried out in the community since there may be a high rate of turnover among these workers.

In the long run, most of the antibiotic treatment must be carried out by the affected population itself. To do this, the people must understand the disease and what measures can be taken against it. An antibiotic treatment programs, the mothers of young children are the prime target for health education since they must be responsible for treating their own children.

The selection of target populations is a critical step in trachoma control programs. Since antibiotic treatment may produce dramatic alterations in the inflammatory disease, the needs of each community are constantly changing and must be reviewed at regular intervals. In communities where individuals suffer from a substantial amount of potentially disabling scars, new cases of trichiasis/entropion will continue to appear, so continuing evaluation will be necessary for many years after the active inflammatory trachoma has been controlled in children.

In most industrialized countries, blinding trachoma has ceased to be a problem of public health importance. In other countries where the disease may not be perceived as an important problem even though it exists, the political and financial support for a program of trachoma control is lacking.

Sale or distribution of subsidized antibiotics as a prevention program has been used in North Africa where chlortetracycline ointment is available in tobacco shops at the cost of a package of cigarettes. Such programs do not guarantee that the drug is used appropriately, but it is available to treat acute eye infections. Moreover, the low price makes it less likely that ointment distributed to families will be resold.

Many mass treatment programs are based on antibiotic treatment of school children. Since not all children attend school and active trachoma is so prevalent in preschool children, these programs have had a limited effect.

In communities where most children acquire active trachoma, antibiotic treatment of the population can be achieved by treatment of families. While the disease in individual patients may respond only slowly to intermittent or short-term treatment, the suppression of the chlamydial and other ocular microbial pathogens will result in decreased transmission and a fall in the "burden of infection" in the community.

Complete programs should include family antibiotic treatment, surgical correction of lid deformities, training of village health workers, health education, and continuing program assessment.

Assessment

Trachoma control programs must be monitored to confirm that the various kinds of interventions (antibiotic treatment of children and surgical correction of lid deformities) are actually reaching target populations. Evaluation must also be done to measure the effect of the interventions in terms of changes in potentially blinding eye disease (severe inflammation or conjunctivel scarring) and in the incidence of blinding corneal scarring. Patients who have had corrective lid surgery should be reexamined to evaluate the efficacy and complications of surgical intervention.

The clinical evaluation could be carried out by an experienced observer in an appropriate small sample of households in villages where the control program is underway. Children should be examined for conjunctivitis, intensity of active inflammatory trachoma, and severity of scarring; and adults, for the prevalence of entropion or trichiasis, corneal scarring, or a history of recent lid surgery. The seasonal pattern of epidemics of purulent conjunctivitis should be taken into account in assessing inflammatory trachoma, and sequential assessments in a region should be carried out at about the same season each year.

The efficacy of antibiotic treatment programs in a community should be apparent within a year. In an effective program, there would be less purulent conjunctivitis and fewer cases of moderate and severe intensity trachoma in children under 5 years of age, but some older children might continue to have higher grades of trachoma intensity. Within 2 to 5 years, children under 5 should continue to have milder active trachoma and should have substantially less conjunctival scarring and corneal vascularization than the next older age cohort.

Individuals known to have had surgery for lid deformities should be examined every 6 months to a year to monitor the long-term result of corrective operations. Recurrent lid deformity (inturned lashes) would indicate that the surgical methods need to be revised.

Laboratory tests should show a marked decline in the prevalence of the trachoma agent in conjunctival specimens obtained by swab or spatula. Bacterial cultures to detect the prevalence of pathogenic bacteria are a good indication of how well antibiotic is administered. Specimens should be taken during mass treatment or immediately afterwards from a randomly selected group of children. Tear or serum antibody levels are not useful in monitoring treatment since the presence and titer of specific antibodies correspond so poorly with clinical disease.

The effects of a control program on new cases with potentially blinding lesions (inturned lids) may not be apparent for 5 to 10 years, and the effect on the incidence of blindness may not be seen for 10 to 20 years. While these long-term evaluations should be made, the short-term effects of the control program can be measured by the reduced incidence and prevalence of both inflammatory disease of the conjunctiva, and unoperated or recurrent lid deformities in the population.

Trachoma will continue to cause blindness in endemic regions unaffected by economic development. The technical means to prevent this visual loss are at hand. The initiation of control efforts depends on the perception of the problem by both public health authorities and the affected populations so the political and financial decisions to support control efforts will be made. Such programs will attain their effect by thorough organization, long-term commitment of resources, and careful planning rather than by novel approaches or technological advances. These programs can be maintained only if they are kept within available financial resources by the active participation of the population being treated.

Outside technical assistance is more important in organization of program efforts, although specific items, such as mobile eye units for surgical teams, may be obtained through international aid programs. In the final analysis, trachoma control programs should be considered not only in the narrow context of preventing blindness but as the beginning of a sustained effort to deliver continuing visual health to rural communities.

Appendix

A TERMINOLOGY TO DESCRIBE BOTH THE INTENSITY OF ACTIVE INFLAMMATORY DISEASE AND THE VISUALLY DISABLING SEQUELAE IN TRACHOMA

This is a modification of the present WHO suggested scoring of clinical signs in trachoma.

I. Intensity of Active Inflammatory Trachoma

To describe more precisely the intensity of active trachoma, a trading of active inflammatory disease in the upper tarsal conjunctiva has been devised. This cale is based on scoring the clinical signs, lymphoid follicles (F) and papillary hypertrophy (P) in the conjunctiva of the upper tarsus. This intensity scale consists of four categories: severe, moderate, mild, and insignigicant or inactive.

For scoring upper tarsal follicles, the upper tarsal and conjunctival surface is divided into approximately equal thirds referred to as zones. These zones are divided by two imaginary lines, approximately parallel with the upper tarsal border that curve upward toward their lateral extremities, as viewed on the everted tarsal surface. Zone 1 includes the entire upper tarsal border and adjacent tarsal surface. Zone 3 includes the tarsal conjunctiva adjacent to the central half of the lid margin, and at its center, it covers just less than half the vertical extent of the tarsal surface. Zone 2 occupies the intervening area and extends to the lateral quarters of the lid margin.

The scores for upper tarsal follicles (F) are designated as follows:

F 0 No follicles present.
F 1 Follicles present but no more than 5 follicles in zones 2 and 3 together.
F 2 More follicles than F 1 but fewer than 5 follicles in zone 3.
F 3 Five or more follicles in each of the 3 zones.

The scores for upper tarsal papillary hypertrophy and diffuse infiltration (P) are as follows:

P 1 Minimal: normal deep subconjunctival vessels on the tarsus not obscured.
P 2 Moderate: Normal vessels appear hazy (even when seen by the naked eye).
P 3 Pronounced: Conjunctiva thickened and opaque: normal vessels on the tarsus are hidden.

The scores for follicles and papillary hypertrophy should be recorded and the grading of intensity made by the observer at the time of examination.

2. Irreversible, Visually Disabling Lesions of Trachoma

The potentially disabling lesions are (1) distortion of the eyelids due to conjunctival scarring and (2) trichiasis and/or entropion. Previously trichiasis and/or entropion have been recorded as conjunctival scarring grade 4 (C 4). To emphasize disabling lesions and to provide a more direct indication of the risk, it is useful to record trichiasis/entropion separately from conjunctival scarring.

The disabling lesion is severe central corneal scarring (CC 3). The scores for these irreversible lesions have been modified as follows:

Conjunctival Scarring (C)

C 0 No scarring on the conjunctive.
C 1 Mild: Fine scattered scars on the upper tarsal conjunctiva.
C 2 Moderage: More severe scarring, but without shortening or distortion of the upper tarsus.
C 3 Severe: Scarring with distortion of the upper tarsus.

Trichiasis and/or Entropion (T/E)

T/E 0 No trichiasis or entropion.
T/E 1 Lashes deviated toward the eye but not touching the globe.

T/E 2 Lashes touching the globe but not rubbing on the cornea.
T/E 3 Lashes constantly rubbing on the cornea.

Corneal Scarring (CC)

CC 0 Absent.
CC 1 Minimal or not involving the visual axis, with no visual loss.
CC 2 Moderate scarring involving the visual axis.
CC 3 Severe central scarring with gross visual loss.

The potentially disabling lesions are severe conjunctival scarring with distortion of the upper tarsus (C 3) and any trichiasis an/or entropion (T/E 1, 2, or 3). The disabling lesion is severe central corneal scarring (CC 3).

3. Blinding and Nonblinding Trachoma

In areas where it is endemic, blinding trachoma can be recognized in a population by the presence of persons with severe visual loss due to corneal opacity, and a substantial prevalence of potentially disabling trachomatous lesions, particularly trichiasis/entropion. These irreversible changes probably result from long continued inflammatory disease of moderate or severe intensity.

Nonblinding trachoma may lead to a low prevalence of potentially blinding lesions, but it does not lead to a substantial prevalence of visual loss in a community.

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RABIES

by

George W. Beran

Rabies is an acute central nervous system disease with worldwide distribution. Its major reservoir is in wildlife, but in much of the world it is a public health hazard because of its endemicity in dogs. In endemic areas, serologically demonstrable subclinical infections occur in a percentage of animals. Man is an incidental host only. However, untreated infection almost invariably results in a fatal acute encephalomyelitis.

Rabies in animals and man has been known since ancient times. Both Aristotle and Galen made reference to the disease. It was Pasteur who showed the virus was present in the brains of rabid animals and proved that the etiologic agent was chiefly concentrated in the central nervous system. It was Pasteur, also, who first prepared an infectious material of known and constant virulence from infected brains and spinal cords of rabbits and used this vaccine for immunization against infection in 1885.

Onset of rabies is usually noted with a sense of apprehension, headache, fever, malaise, and indefinite sensory changes which often refer to the site of an earlier local wound inflicted by the bite of a rabid animal. The disease progresses to paresis or paralysis; spasms of the muscles of deglutition or attempts to swallow with resulting fear of water (hydrophobia); and finally delirium and convulsions. The usual duration of illness is two to six days, sometimes longer: death is apparently due to respiratory paralysis.

The etiologic agent is a bullet shaped virus which belongs to the Rhabdoviridae family whose members include at least 30 animal and insect serotypes plus others in plants and fish. The virions are enveloped, have relatively small genomes with single RNA strands which replicate in the cytoplasm. The virus is sensitive to lipid solvents and acids.

At least five rhabdoviruses have been identified in Africa in addition to rabies; at least two are transmissible to human beings. Unique, subclinical canine rabies infections have been frequently recognized in Ethiopia. These findings, plus descriptions of human disease in ancient Egypt which probably was rabies support an African origin for the virus. Rabies is endemic in dogs throughout Africa. Meerkats and yellow mongooses are wildlife reservoir hosts in South Africa and Rhodesia. Rabid jackals have been reported from East Africa.

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Rabies had spread over Europe and most of Asia and had become endemic in dogs by historic times. The arctic fox is considered the major reservoir host across northern U.S.S.R. and Greenland. Norway, Sweden, and most of Finland are relatively isolated from the land mass of Eurasia. These countries developed some measure of control before the disease became endemic and, thus, remain free today. Denmark, which borders Germany on the south, has experienced rabies more frequently. The entry of rabies in foxes was brought under control in the early 1960s. More recently, when rabies spread rapidly across Europe, Denmark managed to maintain a partially effective cordon sanitaire.

Rabies in red foxes, and less frequently in stonemartens and polecats, has been spreading westward from eastern Europe at an accelerating rate since World War II. The disease has recently crossed the Alps into northern Italy and is spreading through France and Switzerland. England, which was free from 1903 until after World War I and again since 1921, has so far maintained this status with rigid quarantine and surveillance efforts. Though on a world basis, rodents do not appear to serve as reservoir or even alternate hosts of rabies; latent rabies has been shown to be vertically transmitted in several species of small feral rodents in Czechoslovakia, Switzerland, and Germany. It has not yet been demonstrated that these rodents act as a source of rabies for other animals or people. Jackals are considered to be reservoir hosts along the eastern Mediteranean Sea, and wolves are found infected from the Caucasus of U.S.S.R. to Iran along the Caspian Sea.

To the East, rabies was an introduced disease in Korea, Japan, Taiwan, and the Philippines; it apparently became established in dogs as the sole reservoir hosts. Japan and Taiwan were able to eradicate the disease by dog immunization and stray dog control in the 1950s. Hong Kong and Singapore, island countries, and three islands of the Philippines where dog rabies eradication programs were carried out have been successfully freed of the disease. To the south of the Himalaya Mountains, rabies is endemic in dogs, jackals, foxes, hyenas, and mongooses. To the southeast, rabies is endemic in dogs and, in some areas, in mongooses and other animals. The disease is still in the process of moving eastward in insular southeast Asia and is not yet established in Timor and West Irian, Indonesia, or in Papua-New Guinea. Australia and New Zealand and the Pacific Islands remain historically free and except for incursions in Tasmania in 1866-1867 and Guam in 1967-1968 have been maintained rabies free.

In the Western Hemisphere, vampire bats are the largest reservoir of rabies from northern Mexico south to northern Argentina. Though not proven until 1908 when bovine rabies (mal de caderas in southern Brazil) was shown to be bat transmitted, the records of Spanish explorers as early as 1415 described deaths in soldiers subsequent to vampire bat bites (Oviedo in Panama). Bovine rabies transmitted by vampire bats was estimated by the Food and Agriculture Organization (FAO) in 1966 to have caused the loss of one million cattle annually. The disease is spreading southward in Argentina with the expansion of the cattle industry. Cattle are the favored hosts for feeding vampire bats. The virus cycles principally in these bats with some extension to cattle and occasional exposure of other animals and people. Urban dogs, and to a lesser extent urban cats, are the major reservoir hosts for exposure of human beings from Mexico south. Other animal hosts in Latin America include the mongoose from Puerto Rico and eastern Cuba through the western islands of the West Indies, foxes, raccoons, coyotes, and skunks.

In North America, the dog has been controlled as a reservoir host through extensive immunization and the animal control programs: it remains important in the epidemiology of the disease only along the southern border with Mexico. Rabies is widespread over North America in insectivorous bats. In certain cave environments in southwestern U S. with high concentrations of colonial bats, airborne transmission to a variety of animal species has been shown to occur experimentally. Rabies was demonstrated to have occurred naturally in humans in at least two instances. Vertical transmission of rabies virus has been demonstrated in insectivorous bats. Three major wildlife reservoir hosts are important in maintaining endemic rabies throughout the U.S. Red and grey foxes are important in the eastern U.S. from New York State through the Ohio River Valley and Appalachia and along the coast of the Gulf of Mexico and eastern Texas. Skunk rabies is endemic in a belt from north to south along the Mississippi River Valley and each year moves farther west into the great plains. Another focus of skunk and fox rabies exists in California. Raccoon rabies is endemic in an expanding focus in northern Florida, eastern Alabama, Georgia, and southern South Carolina.

Rabies in domestic animals in Mid-western U.S. is largely due to exposure by skunks: canine rabies is commonly traced to wildlife exposure in the endemic areas of skunk, fox, and raccoon rabies. Across Alaska and northern Canada, rabies is endemic in arctic foxes, which transmit the disease to wolves, coyotes, and occasionally, to sled dogs. Human exposure is not common probably because of infrequent contact with foxes and the heavy protective clothing commonly worn by people in colder climates.

Assessment of the Reservoir Population

Target dog populations for immunization or population control must be estimated or enumerated. These animals are seldom registered in any country and densities commonly vary widely by geographical area. Dog populations are commonly estimated as a proportion of the human population. Such calculations must be made by areas of the country. In large urban centers, if dogs are owned and quartered by individual families and human population censuses are reasonably accurate, a door to door survey of 10% of the households may be sufficient to generate a good estimate of the dog/human population ratio. In many cities, several homogeneous districts must be surveyed separately for estimates to be reasonably accurate. These districts include urban commercial areas where second floor dwellings above shops are found; urban residential areas which contain multiple family dwellings; suburban residential; and refugee or squatter settlement areas. The dog/human population ratios for these districts should be applied to the proportion or the urban population contributed by each district.

In village areas, dogs may range with minimal inhibitions through part or all of a community, and ownership is less specific than in a city. A dog/human population ratio may be estimated by physically counting the dogs seen and the people residing in the dwellings in a surveyed area. Such a count, based on 10% of the inhabited portion of each of 10 villages in relatively homogeneous occupational-linguistic areas, can give a highly accurate dog/human population ratio as well as an indication of the validity of available human census data. Fishing villages may have a very different composition from rice, corn farming or commercial farming villages such as sugar cane plantation areas. In scattered rural dwellings, isolated mountain, forest, or nomadic temporary settlements, human censuses are seldom accurate and dog populations are composed of both owned dogs and roving bands of dogs. Unless such settlements comprise over 10% of the human population in the projected rabies control areas, it is probably workable to use only a general estimate of the dog population for planning, but it is then essential that these dogs be reached in the immunization or population control campaigns.

Areas within a country which differ in language or religion, even in agriculturally homogeneous regions, may have significantly different social customs and attitudes toward dogs and other animals. Areas in which dogs are consumed for food may have lower overall dog densities but may have equivalent dog rabies problems in mangy or otherwise undesirable, free roaming dogs. Moslem areas may have much lower dog populations than Buddhist or Christian areas of a country.

Other domesticated animals--cats, cattle, swine, and horses--act more as alternate hosts than as reservoir hosts of rabies. Except perhaps in urban centers of high cat populations, the disease tends to disappear in cats in the absence of rabies in dogs and other animals. In urban centers, cats can be estimated by door to door surveys as can dogs. In village and rural areas, unless cats are continually exposed to wildlife reservoirs of rabies, they can probably be excluded in rabies control programs. Livestock are important indicators of the presence of rabies reservoirs in an area, but except for the transmission of rabies to cattle by vampire bats, primary control efforts are seldom based on protection of livestock.

Wildlife must be assessed both on their actual (rather than potential) roles as reservoir hosts and on their population distribution. Rodents can be excluded from consideration. Vampire bats must be considered in Central and tropical South America; insectivorous bats throughout the western hemisphere; but in the eastern hemisphere, should be considered only if there is specific evidence of bat rabies in the region. Periodic reports of bat rabies in Asia have not been confirmed. Wild canines (dogs, wolves, jackals, foxes), mustelidae (weasles, minks, otters, badgers, skunks), and viverridae (civets, mongooses, and other small carnivores) must be given serious consideration as reservoir hosts wherever they exist.

Basic Considerations in Rabies Control

In the developing countries, rabies is but another health hazard in a burdensome array of infectious and parasitic diseases. People who live in interior areas without local medical care or means to get to medical care live in fear of all animal bites and largely equate all bites with exposure to rabies. An extensive folk medicine for the prevention of rabies in bite victims has grown up. It has been fostered by the development of rabies in some animal bite victims. Even as medical care gradually became available, physicians had no practical access to animal diagnostis services. Faced with the possibility of a patient's exposure to rabies, physicians administer vaccine to nearly all bite victims. At best, vaccines available to these physicians are 80% protective. The antigens suffer also from adverse conditions during transport, storage, and delivery so that vaccine administration following exposure may be greatly delayed. Thus, the apparent incidence of rabies in animal bite victims treated by folk medicine or by modern medicine may not be notably different in the eyes of rural residents.

In urban areas of developing countries, medical care and diagnostic facilities may be considerably better, but prophylactic care of animal bite victims is still complex and only partially effective. Human rabies is one of the most terrifying and horrendous of all infectious diseases: it completely disrupts family structure and stability. Family members and attendants are frequently suspected of having been exposed by clinical patients, and whether valid or not, this belief perpetuates fear of the disease.

In countries with a primary dog rabies reservoir, the elimination of endemic rabies may be achieved by measures which are practical within the social structure and without pain or risk to community residents. Achievement of rabies control removes this important health burden from society, enhances the status of public health and medicine, and may be the prototype for community acceptance of preventive medicine. It may open the door to success in mass immunization programs for control of childhood diseases or cooperation in mass parasite control programs. In countries with epidemiologically important wildlife reservoirs of rabies, control may be more difficult. Yet, the dog reservoir may be the significant hazard for human exposure so that control of dog rabies may still be a dramatic public health measure.

Rabies control programs must be based on a knowledge of the epidemiology of the disease in a specific country. Neither data nor procedures applicable to one country can be transferred to another. Essential are data on the reservoir host range; the population density and distribution of dogs and other important animal hosts; patterns of dog and other domestic animal ownership in urban and rural areas of the country; and social patterns which influence transmission of the virus. Based on assessment of the epidemiology of the disease, decisions must be made about whether the objectives of rabies control will be

(1) to reduce the risk of individual exposure;
(2) to achieve rabies control in limited areas, such as points of population concentration, and therefore, reduce human exposure on a wider basis;
(3) to eradicate rabies from limited areas, with projection toward expansion of rabies free areas; or
(4) to systematically implement eradication on a national level.

Development of a Rabies Control Program

The strategy and implementation of rabies control programs,

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though they have many common aspects, must be adapted to local conditions. Some form of governmental decree or sponsorship is essential for a successful program; the sponsor may be the national government for a nationwide program or the government of a subunit for a provincial, state, or even city program. A legislative act or executive decree should stipulate officially the need for regulations and procedures for animal ownership, registration, movement, immunization, the action to be taken for noncompliance, and the enforcement authorization. A model for a national decree in a developing country with a dog rabies reservoir problem is attached as Appendix 1.

Public acceptance of rabies control develops with public understanding of its importance and effectiveness. An extensive educational program for health professionals and the public is needed. Professional information on the cycle of transmission, on proper handling of animal bite victims, and diagnostic procedures and criteria must be made available to public health officials and physicians. Veterinary service personnel, public and private, must be provided with information on animal reservoirs of rabies and on their role in diagnosis. It is important that physicians and veterinarians share information and that they be involved in public education along with governmental education staff. Articles on rabies in newspapers and magazines, features about rabies on radio and perhaps on television, widespread displays of posters in public locations, and printed handouts may all be used. These media can inform the public of the hazard of rabies, of proper measures to protect animals from the disease, and how to prevent rabies transmission to people. All efforts must be directed toward obtaining public participation in the program of animal immunization and population control.

In planning a coordinated rabies control program, the authorities and representatives of agencies which may be involved should hold a working conference early in the development of the project to educate participants to the need for the program and involve those present in its planning and implementation. If the program is to be nationally sponsored, the participants should include representatives of the following agencies:

- ministry of public health, particularly the divisions of health services, laboratory services and disease surveillance;
- ministry of agriculture and its division of veterinary services;
- ministry of education;
- ministry of finance;
- immigration and quarantine office;
- ministry of defense in countries with a centralized police service;
- national representatives of the World Health Organization and the United Nations Development Program; and
- representatives of interested international development or aid missions.

Out of this planning conference, a coordinating committee may be appointed by the prime minister or other national official. The principal coordinating official or director of the program will probably be the director of veterinary services or the director of public health services or one of their representatives. This official will convene the coordinating committee and will function as enabler of the dog immunization and animal population control phases of the programs at provincial and city levels. A committee that represents provincial and city health, veterinary offices, and local government boards should be formed as the program moves into these areas.

If a rabies control program is to be initiated and developed at a provincial or city level, the planning conference should include the provincial governor or city mayor and appropriate provincial or city officials. Special campaigns and ongoing programs must involve governmental units at the lowest level for which program activities are planned--e.g., at the national, regional, county, city, or provincial levels.

Immunization programs coordinated at the national level usually require a minimum staff of four full time coordinators. The director handles administrative planning with local government officials from areas where campaigns are to be conducted and coordinates laboratory and field activities. A supply and records officer handles shipments of vaccine and supplies to field units and maintains central records of animals given rabies vaccine as reported back by field units. A field officer works with field units in requesting, receiving, and distributing vaccines and supplies; scheduling immunization clinics and house-to-house campaigns; receiving reports for consolidation and submission to local government officials; and forwarding reports to the central supply and records officer. A training officer works ahead of active field units, training local personnel in the next towns or administrative jurisdictions in preparation for the next field unit campaigns.

Immunization programs coordinated at the provincial or city level can usually be conducted with two to three coordinators who are assigned to temporary duty for the duration of projects. The director handles planning and scheduling. A supply and records officer handles logistical support for local immunization teams and records field reports of animals immunized. A training officer trains field personnel; the director may perform this training function in relatively small programs.

The field officer must have a vehicle for transporting vaccine and supplies from the local supply center to field units; in some instances, for transporting immunization teams to operational centers; and for taking back requests and records. In countries with contiguous land routes, this vehicle may be assigned from the national center, but where water or mountain barriers preclude direct travel to field areas, it may be necessary that vehicles at such sites be temporarily assigned to the field officer.

An immunization team is conveniently composed of three persons, one of whom functions in animal holding, one in administering vaccine, and one in recording information. Team members may rotate in these functions. Immunization teams may be organized on the basis of estimated number of animals with a team of three persons able to immunize an average of 100 dogs per working day in sparsely populated rural areas and about 200 dogs in urban centers. Staff to administer the vaccine can often be recruited temporarily from local health, veterinary, and community development agencies. These persons know the local languages or dialects, the local villages and people, and have a real personal stake in the benefits of a successful project. The added costs in training and outfitting new field personnel in each campaign area compared with assigning staff from the national center are far outweighed by the efficacy of local personnel. These persons should receive adequate training to prepare them to perform their task as well as to explain and promote the immunization program. They should be given pre-exposure rabies immunization with a human vaccine authorized for this use; this can be given in conjunction with the training program.

Each team needs a kit composed of a small polystyrene ice chest for vaccine and diluent, sterile syringes, and sterile needles. Plastic, disposable 2½ ml. syringes of the type which may be rewashed and boiled or autoclaved 25 or more times without excessive warping are both convenient and economical. A new supply of sterile syringes and needles must be ready for each day. If autoclaving facilities are available, sterile syringes and needles may be exchanged for used items daily by the field officer and taken back for autoclaving. If not, the staff may be instructed in boiling syringes and needles and instructed to handle their own items daily. A small jar of alcohol pledgets must be provided. A bamboo handled dog catcher and holder, which has a one cm diameter rope loop attached at one end of the handle and threaded through the hollow tube so that it may be tightened over dogs' necks, is essential for handling otherwise unmanageable dogs. Numbered dog tags are desirable but not essential. Plastic tubing threaded with light wire produces an effective dog collar to identify annimals who received vaccine. Registration and immunization records should be provided for completion in triplicate. A sample immunization certificate and registration form is attached as Appendix 2.

Dog, cat and bovine immunization programs must commonly utilize a central supply of vaccine. Except for initial or pilot projects or for small countries, production of vaccine within the country is probably the only economically feasible source. Inactivated vaccine of brain tissue origin are relatively easy and economical to produce, and the capability for such production exists in many countries throughout the world. However, the immunity elicited by these vaccines is of short duration and their application very limited for use in large campaigns with costly delivery logistics. Attenuated live Flury strain vaccine produced in embryonated hens' eggs requires greater aseptic technique and more complex technical control at all steps in production, but can be produced in large quantities at relatively low cost with a relatively low investment in equipment. Furthermore, it provides an effective immune period of at least three years. A guide for the production of the vaccine is included in the World Health Organization (WHO) Monograph series No. 23, Laboratory Techniques in Rabies, 1973. A detailed vaccine production protocol which contains a list of equipment and annual supplies for a unit with a capacity of 500,000 doses per year has been prepared by this author for WHO and is available by direct request to WHO Headquarters, Geneva, Switzerland, or to this author.

Inactivated vaccine of suckling mouse brain tissue origin is produced on a large scale in several developing countries and has an effective immune period of two to three years. A guide for production of this vaccine is also included in the World Health

Organization Monograph. The recently developed cell culture origin vaccines require rather highly skilled technical personnel and a high degree of technical control but utilize a relatively small investment in equipment and supplies. It is probably essential that anyone who supervises a laboratory for production of cell-culture-origin vaccine study in an experienced laboratory that produces such a product.

Delivery from the central laboratory to field units must be both dependable and performed under conditions which ensure the maintenance of vaccine potency. Where available, local refrigerator units with storage capacity for one to two weeks anticipated vaccine needs are valuable, but the dependability of the refrigeration must be ascertained beforehand. Air freight services are available to provincial cities in most developing countries, and shipment of vaccine on ice in polystyrene chests by air is generally most satisfactory.

Development of a Pilot Rabies Immunization Campaign

Prior to the initiation of any large scale immunization program, one or more small pilot projects should be conducted in geographically delineated areas. Assignment of personnel, logistical support, scheduling, and public information can all be worked out through such projects.

National or regional campaigns are best organized in stepwise fashion through use of natural barriers to animal movement, such as islands, rivers, mountains, or unpopulated areas, to protect immunization zones from the entry of rabid animals until dogs in adjacent areas receive vaccine. In urban centers and villages, immunization clinics can be organized to which people bring pet animals for immunization, registration, and identification. The success of such clinics vary and will not reach free roaming dogs, self-sustaining dogs, vicious or unmanageable dogs, and dogs whose owners are absent from the premises. After a clinic has been held, house-to-house visits must be made to immunize unmarked dogs. Frequently the immunization teams are required to capture the dogs before giving them vaccine. It is essential that at least 80% of the dogs over three months of age in any area be immunized in order to break the cycle of rabies.

The control of free roaming animals, especially in villages and rural areas of developing countries is often very difficult to achieve, and the extent to which it may be accomplished must be maximized for each control program. It is frequently more sociologically feasible for teams to capture and give vaccine to free roaming dogs in a community than to destroy such animals. Pounds for holding stray animals are out of the question except in the largest cities. The population of free roaming dogs is commonly at, or slightly above, the carrying capacity of the available food supply, and removal of dogs leads only to their being replaced almost immediately from the periphery. Immunization and release of the existing dogs will actually help to prevent a rapid buildup of unimmunized dogs in communities at the campaign boundaries.

Efforts to protect newly immunized communities from the entry of dogs from unimmunized areas include:

- development of stepwise campaigns which make maximum protective use of natural barriers;

- education of people in the importance of moving only immunized dogs will have a pronounced effect if vaccine is available to such owners;
- placement of a supply of vaccine, syringes, and needles;
- designation of an immunization authority at a convenient center in each municipality;
- dissemination of public information on this service;
- enlistment of community residents to help inform incoming persons with dogs about the availability of vaccine.

In urban centers, leash laws, dog catchers, dog tags, and enforcement of immunization requirements are much more feasible and should be fully utilized.

When national dog immunization programs are undertaken, the stepwise coverage of the country should not take more than three years: if it can be done in a shorter time, there is a greater likelihood of preventing re-entry of rabid dogs from unimmunized areas.

Continuation of the immunization program after completing national coverage will depend on the epidemiology of rabies in the country. If national coverage was not complete, a second campaign should be conducted within 12 months in those areas not fully protected. In countries with a wildlife rabies reservoir, annual program activities should include immunization of all puppies which have reached three months of age and all other dogs not previously immunized as well as reimmunization of immunized dogs after three years. Countries which have common boundaries with rabies endemic countries must annually give vaccine to all dogs not previously immunized in a buffer zone at least 10 miles deep.

It is, of course, most effective in any country at risk of rabies re-entry to regularly give vaccine and to reimmunize. It may, however, be far more economically feasible to maintain protection at ports of entry by requiring immunization certificates plus quarantine. A continual surveillance program must function on a national basis. For several years after the national immunization campaign, a cafre of experienced vaccine teams should be available in all areas. A central stock of vaccine and supplies should be maintained. At the first recognition of a case of rabies in any species, an immediate saturation reimmunization program should be carried out within and around the periphery of the affected area.

In developing countries, the cost of rabies control must be borne largely by government. The program is based on uniform participation throughout the nation. Animal owners cannot be refused immunization if they cannot pay for it; neither can unowned dogs be left unimmunized in a community. In urban areas, many dog owners are able and willing to pay for private immunization of their pets. Government sponsored clinics, however, must be available to all owners whether able to pay or not.

Records of animals immunized should be kept both at local and national centers. At local levels, such records are needed for medical determination of appropriate care of animal bite patients. At national levels, operation and assessment of the program will be based on field records.

National Benefits of Rabies Control

The direct costs of rabies to a country include the human lives lost, usually young people; the animals lost, especially in work and food producing animals; the travel expenses and medical care of animal bite victims; and their time lost from work. These are all major expenses; and in most developing countries, the medical care must be borne at public expense. It may be feasible to underwrite the costs of a rabies control program in countries with a primary dog reservoir on a purely economic basis. This is estimated to be true for the national rabies eradication program now in progress in the Philippines. The cost-benefits of the Philippine program as calculated in 1976 for the World Health Organization are shown in Appendix 3. It was estimated that the cost of eradication would be recovered in approximately 2½ years through the elimination of required medical care for the animal bite victims and rabies patients. Costs would be increased and benefits reduced in countries where wildlife reservoirs of rabies necessitate a continual dog rabies vaccine program and where a wildlife reservoir constitutes a continuing risk to humans and dogs. However, the additional economic burden would still be well worthwhile as a public health measure.

The indirect costs of rabies to a country include the mental stress incident to animal bite exposures; the pain and inconvenience of postexposure prophylaxis; the disruption of family and community stability caused by human and, to a lesser extent, by animal cases; and the loss of faith in medical services attendant on failure of prophylactic immunization to protect victims from rabies. It is important also to eliminate these social consequences of rabies especially in rural areas of developing countries. Indeed, the successful control of rabies when it is publicly evident in such areas may result in the following:

(1) promote public participation in other preventive measures,
(2) promote the transition from folk medicine to acceptance of modern medicine, and
(3) accelerate technological development and tourism by removing the fear of visiting areas once considered hazardous because of endemic rabies.

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Appendix 1

A Model for a

NATIONAL RABIES CONTROL

LAW or DECREE

Be it (enacted or decreed) by the (governing body) that:

Section 1. The (area of county) of (state of province) shall be declared a rabies control area, and appropriate actions thereto shall be taken.

Section 2. Mass dog vaccine clinics shall be conducted throughout the (area of province). Antirabies vaccine recognized to provide immunity for a minimum period of three years shall be used, and all dogs three months of age and older shall be immunized.

Section 3. All dogs who receive vaccine shall be registered and suitably identified as immunized. Standard registration forms certifying the effective immune and the registration periods shall be completed in triplicate. The original shall be provided to the owner and the copies sent to (pertinent health and program authorities).

Section 4. The conduct of immunization campaigns and the registration of dogs who have received vaccine shall be under the supervision of (Director of Veterinary Services or other authority) with the cooperation of (other pertinent government agencies).

Section 5. Following mass immunization campaigns, all dogs found outside owners' premises without proper identification as having received vaccine shall be considered stray dogs.

Section 6. Stray dogs shall be given vaccine and brought under control by appropriate means or humanely destroyed.

Section 7. (Applicable where the control area is less than the entire nation.) Any dogs entering the control area from unimmunized areas must either receive vaccine within three days of entry from the __(Veterinary Services)____, or be quarantined at the owners' residences for 30 days, and then be reimmunized before registration unless previously immunized as defined in Section 2.

Section 8. All dogs brought into the control area across international borders must be accompanied by certificates of proper antirabies immunization as defined in Section 2, performed not less than one and not more than twelve months prior to entry. Dogs not so immunized shall be given vaccine at the port of entry, quarantined for 30 days, and reimmunized before registration. This authority shall be vested in the ____.

Section 9. Antirabies immunization and registration of immunized dogs shall be performed without charge for dog owners.

or alternate Section 9. Dog owners shall be assessed the amount of ______________________ for each dog immunized and registered with official receipts issued at the time of payment. Dog owners unable to pay shall be provided immunization and registration without charge. No dog owner may be exempted from having his/her dog(s) immunized and registered by refusing to pay.

Section 10. This act shall repeal and supercede all previous acts which are in any way contrary to this _(law or decree)_______________.

Section 11. Any persons violating any provision(s) of this act shall be subject to ______________________________.

Section 12. This act shall take effect on ____________ and shall continue in effect until superceded by ____________ ____________________.

Appendix 2

A Model for a

DOG REGISTRATION FORM
(Issue in Triplicate)

Dog Registration Rabies Control Program

Owner's Name ______________________ Registration No. ________

Address ________________________ Dog Tag No. __________

Description of Dog:

Breed______________ Color __________ Sex _____ Age ___

Name ______________ Weight __________ Condition ________

Vaccine Lot No. ________ Date Injected ______ Date Registered ________

Vaccine Immune Period __________ Registration Expires __________

____
Vaccinator-Registrar

Appendix 3

COST-BENEFITS OF RABIES ERADICATION

Based on the Philippine Program, 1976
Figures in Philippine Pesos (₱)

At the present time, approximately 100,000 people annually receive either a partial or complete series of post-exposure, prophylactic rabies vaccine injections. At least 90% of the vaccine is supplied by the Bureau of Research and Laboratories. Approximately 200 human rabies deaths are recorded each year. Most of the exposures and deaths occur in rural areas with over 50% in persons 12 years of age or younger. The following cost-benefit analysis is based on data collected in the Philippines; projected costs are based on 1976 prices. The value of animals lost because of rabies is included for food animals only, exclusive of their salvage value.

Economic Costs of Rabies Per Year

Immunization of 100,000 people	
Cost of vaccine 90% Sample, 10% Duck Embryo	₱ 3,250,000
Medical care costs	1,500,000
Work time lost in obtaining vaccine or transporting children	1,500,000
Travel expenses by patients	2,800,000
Added medical care costs due to postvaccinal reactions	20,000
Deaths of 200 people	
Cost of hospital care, average 3 days each	60,000
Family costs for work loss	20,000
Travel costs for patient and family	12,000
Loss of life at ₱10,000 per death	2,000,000
Livestock losses less salvage value	158,000
	₱ 11,320,000

Economic Costs of Rabies Immunization Nationwide

Immunization of 5,000,000 dogs	
Cost of vaccine at ₱3.00 per dose	₱ 15,000,000
Delivery of vaccine from laboratory to local areas	500,000
Immunization supplies	750,000
Labor costs for immunization teams	3,000,000
Travel costs for immunization teams	750,000
Locally borne costs for immunization teams (food, lodging, etc.)	750,000
Local costs for dog owners (travel, work loss, etc.)	3,500,000
Administrative costs for immunization program	1,250,000
Control of dog movement, quarantine	2,500.000
Total Cost of Dog Vaccine Program	₱ 28,000,000

The cost of rabies eradication by dog immunization is approximately 2½ times the yearly economic costs of endemic rabies.

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FILARIASIS

by

Robert S. Desowitz

Filariasis is due to the lymphatic-dwelling parasites Wuchereria bancrofti and Brugia malayi and may well be the most "visible" of all tropical infections. While the diseases that comprise "tropical medicine" contribute numerous models to the clinical Chambers of Horrors, few are more pitifully dramatic than the crippling disfigurements of filarial elephantiasis.

Filariasis in its broadest connotation means infection with one of several species of filarial worms. This paper will be restricted to the surveillance and control of human infections due to the hematode worms Wuchereria bancrofti and Brugia malayi. These infections are transmitted from man to man by a variety of mosquito species.

Both male and female adult worms are found coiled in the lymphatics, usually in the deep lymphatics of the inguinal and pelvic regions. Female worms discharge microfilariae (active embryos) into the lymphatics and they eventually make their way to the blood stream. Once in the circulation, the microfilariae may live for weeks or months and apparently some as long as a year. In most areas of the world where these infections occur, the microfilariae show a well defined nocturnal periodicity in the peripheral circulation; they are most plentiful from about 10 p.m. to 2 a.m. and except in very heavy infections may not be found at all at midday. Microfilariae picked up by a mosquito while feeding on an infected person penetrate the stomach wall of the mosquito, lodge in thoracic muscles, develop into infective larvae which then migrate to the proboscis. This mosquito cycle takes about 10 days and the infective larvae are then transmitted to a new human host when the mosquito bites.

Many infected persons show no clinical signs or symptoms. Early acute manifestations may include fever, lymphadenitis, lymphangitis of the extremities, orchitis, epididymitis, funiculitis, and abscess.

No significant permanent damage results from the initial infections nor even from a considerable number of reinfections and superinfection. However, when the host continues to be exposed to infection for many decades, the increasing inflamation and fibrosis of the lymph nodes with recurrent edema results in celular infiltration with permanent tissue enlargement. The result is elephantiasis

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of the limbs, genitalia or breasts, or chyluria.

Elephantiasis represents only the tip of the clinical iceberg and a still smaller proportion of the infected population. Less than 5% of adults and rarely as much as 10% in a highly endemic setting develop elephantiasis. The range of clinical manifestations, which include psychological aberrations, attributed to filarial infection is so great that it may be thought of as a mimic of malaria which, in turn, has been called "The Great Mimic." Clinical manifestations are due to an inflammatory response of the lymphatics which react to the adult worm and are expressed as lymphadenitis, lymphagitis, lymphedema, chyluria, and in males, orchitis, epididymitis, enlargement of the spermatic cord, hydrocala, and lymphoscrotum. Recurrent "filarial fever" is another manifestation that can be of sufficient severity to send an allicted individual to his/her bed repeatedly for several days at a time.

Tropical eosinophilic lung (TEL) is believed to be a hypersensitivity to the microfilariae of W. bancrofti although the etiology and immunopathophysiological mechanism have not as yet been completely elucidated. TEL occurs mainly in Indians exposed to filariasis. Clinicians and filariasis workers in Southern India consider TEL to be a relatively common syndrome in that region of the country.

Surprisingly, the great majority of individuals with microfilaremia seem to be either unaffected by the parasite or give no history of filarial disease. However, the notion that filariasis is essentially a benign infection may not be true. Filariasis is an infection of lower urban socioeconomic classes and of "simpler," rural socioeconomic populations. These people are so often beset by a variety of infections and other diseases that illness becomes an accepted component of life. It may be difficult to perceive illness when one is never truly well. Fevers are so common that the identification of fever of filarial origin is extremely difficult. The continual assault of disease leads to what may be called "cultural indifference." A study carried out in Tonga (Desowitz, Berman and Puloka, 1977) in a setting of hyperendemic, sub-periodic Bancroftian filariasis demonstrates this phenomenon. History taking elicited relatively few complaints associated with filarial infection. Yet when physical examinations were carried out over 50% of adult males were found to have hydrocele. When questioned further, the affected individuals felt that hydrocele was so common it was not worth mentioning.

The problems of cultural indifference and the nonspecific nature of filarial symptoms have led to difficulties in evaluating the impact of filariasis on a community. The effect of filariasis on the economy of an endemic region has not been investigated as has been attempted for malaria and schistosomiasis. Some twenty years ago, filariasis workers at the Malayan Institute of Medical Research estimated that work loss resulting from filarial fevers and episodic acute lymphatic inflammation led to a decrease of 10% to 15% of that country's rubber production.

The World Health Organization estimates that approximately 250 million people throughout the world are infected with W. bancrofti/B. malayi. This figure is undoubtedly too modest and the prevalence is probably two to three times 250 million.

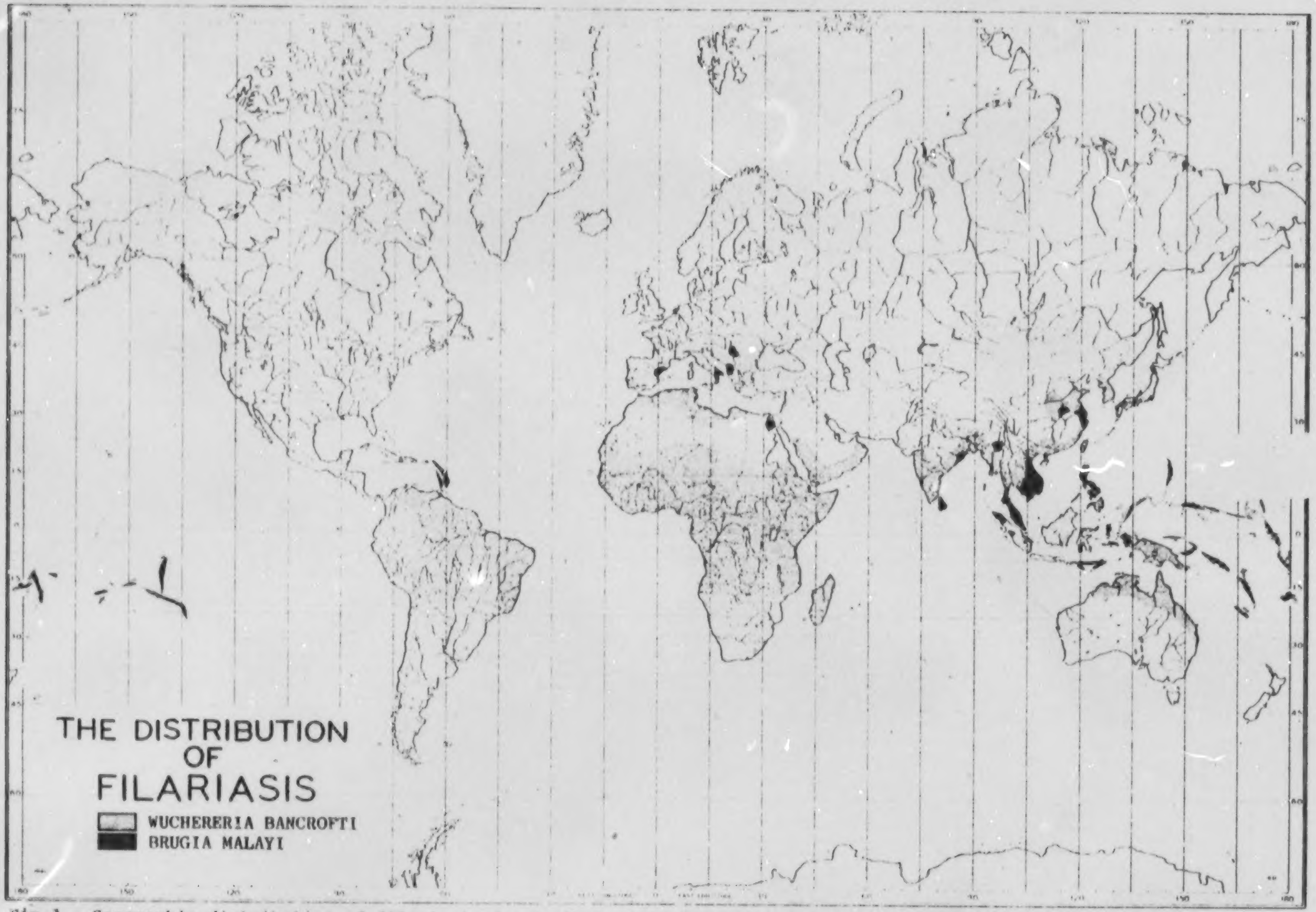
THE DISTRIBUTION
OF
FILARIASIS
▨ WUCHERERIA BANCROFTI
■ BRUGIA MALAYI

Fig. 1 - Geographic distribution of filariasis due to *Wuchereria bancrofti* and *Brugia malayi*.

The underestimate of world filariasis prevalence occurs because the estimate is based on data derived from surveys using the "classical" 20 mm^3 stained thick-blood film. The development and application of a more sensitive technique-membrane filtration (MFC)--suitable for field use has revealed twice as many microfilaremias as formerly noted in adult age groups and as high as seven to eight times the 20 mm^3 mf rate in children. Also, the prevalence calculations are based on a population estimate made some 20-30 years ago. Since then the world population has increased by 58% and the greatest contribution to this population growth has come from the underdeveloped, tropical regions.

Effective filariasis control has been accomplished in very few countries. By contrast, human activities such as rapid, uncontrolled growth of tropical cities have led to conditions which are conducive to the breeding of misquito vectors and that, in turn, has intensified the spread of filariasis. In India where filariasis was once believed to be confined to the coastal regions, transmission now occurs in all but two states.

With the exception of desert ecosystems, filariasis occurs in virtually every region of the tropics. Major foci exist in Asia, Africa, South and Central America, Melanesia, Micronesia, and Polynesia. Comprehensive reviews of regional epidemiology have been given in the recent book by Sasa (1976), the reviews by Hawking and Hawking and Denham presented as WHO unpublished documents (1971-75 and abstracted Annex 1 in WHO Expert Committee on Filariasis 1974 report). A comprehensive report on the current status of filariasis in the Polynesian-Micronesian region was prepared by Desowitz in 1975 for the U.S. Army Medical Intelligence Agency and may be available upon request to government and other organizations.

Planning and Evaluation of Surveillance and Control

A logical, effective antifilariasis program must be based on a firm understanding of those factors which contribute to the spidemiology of the infection in any particular locale. The complexity of these interrelations is illustrated in the table on page 155, which lists the components and factors influencing transmission of filariasis.

Not only is identification of the vector(s) important but, equally crucial is an understanding of the elements of both human and vector behavior that act as centripetal forces of contact. Moreover, these behaviors must be considered within the ecological areas in which interaction takes place. In terms of "landscape epidemiology," filariasis can be broadly characterized into urban- and rural-related infections. Urban filariasis is due to the periodic form of W. bancrofti transmitted by Culex faticans. Rural filariasis is a complex of periodic and subperiodic W. bancrofti and B. malayi transmitted by aedine, anopheline, and Mansonia mosquitoes. The ecosystems and environmental habitats of rural filariasis are diverse; high and low island, tropical humid forest, swamp forest, and savanna.

With notable exceptions, most countries in the endemic zone have tended to neglect filariasis as a target for intensive control measures. Faced with deficiencies in medical personnel,

COMPONENTS AND FACTORS INFLUENCING TRANSMISSION OF BANCROFTIAN FILARIASIS

Component in Transmission/Life Cycle	Factors
Microfilarias (mf)	1. Number of mf in peripheral blood
	2. Life span of mf
	3. Periodicity of mf
Vector	1. Number of species of suitable vectors
	2. Bionomics: ecological conditions peculiar to breeding and survival of vector
	3. Geographical range of vector(s)
	4. Vector population and densities
	5. Vector life span
	6. Vector flight range
Vector-Host	1. Host predilection of vector, e.g., man or animal, age of host, other host factors.
	2. Host-vector contact a. activities of man that brings him in contact with vector b. activities of man that contribute to breeding conditions of vector
	3. Amount of blood vector ingests
	4. Other feeding havits of vector, e.g., frequency, time, etc.
Vector-Parasite	1. Vector efficiency
	2. Number of mf ingested
	3. Effect of developing larvae on vector a. life span of vector b. biting habits of vector c. flight range of vector
Host-Parasite	1. Number of infective larvae required to produce patient infection
	2. Number of infective larvae required to produce clinical manifestations
	3. Effect of immune response on parasite
	4. Other host factors

equipment, and funds, the underdeveloped countries have concentrated their efforts on public health campaigns to combat potentially life-threatening infections, such as malaria and/or infections, for which relatively simple and cost-effective measures are available, such as certain immunization programs. Given the opportunity and support, many governments would undertake antifilariasis measures if convinced that there is a compelling need to do so. The argument must be presented in understandable, quantitative terms of prevalence of infection, extent of disease induced by infection, and if possible, an estimate of the economic and social impact of the disease on affected communities and nations. There must, of course, also be persuasive argument for the effectiveness of an antifilariasis campaign.

The new techniques for detection of microfilaremia produce a much clearer and more accurate picture of the endemic level. Whenever possible, sample surveys using these diagnostic methods should be carried out to obtain more accurate estimate for presentation to national authorities. Since it has been shown that clinical manifestations are not necessarily related to degree of microfilaremia (Desowitz, Bermand, and Puloka, 1977, and references cited therein), inclusion of low-grade microfilaremias diagnosed by membrane filtration in the total microfilaremia rate is appropriate. As noted earlier, difficulties exist in obtaining accurate disease rates. Paramedical personnel can obtain an elephantiasis rate readily to use as one measure of disease if it is clearly understood that an elephantiasis rate represents only a narrow portion of the clinical spectrum.

Antifilariasis programs are not plagued with many of the technical difficulties associated with antimalaria campaigns. However, like all other public health programs, once a decision has been made to institute an antifilariasis program, the essential problems reduce to who will carry it out and how much will it cost. There are two operational components to antifilariasis programs: field staff responsible for carrying out antifiliariasis measures; and laboratory staff responsible for technical aspects of surveillance and evaluation.

All personnel require initial training and, later, facilities and materials to carry out their responsibilities. Countries within the endemic zone (see map, page 153) differ greatly in such resources as medical, paramedical, and nontechnical personnel. The complexity of any campaign will depend upon the size and nature of this personnel pool and the funds national authorities are willing to allocate to filariasis activities. Technical and other resources should be assessed before any program plans are developed. Assessment of resources should not be limited to government employees but should include academic experts in filariasis studies and those specialists available from supranational organizations, such as WHO and AID. An analysis should also be made of national and community public health programs into which an antifilariasis campaign can potentially be integrated. Moreover, plans for such a campaign must be cognizant of the administrative character of the country's health activities. Are health programs centralized or decentralized at the provincial or state level? If decentralized, what are the interrelationships (fiscally, technically, operationally) between national and provincial health departments.

Estimate of the Current Problem from Existing Sources of Data

This section discusses the extent and reliability of available data on filariasis in countries in the endemic zone. Generally, information is adequate to identify most endemic areas and foci and to provide some estimate of the endemic level. Where

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an active antifilariasis program exists, data can usually be obtained from laboratory records and annual reports; occasionally from publications in scientific journals. Accuracy, completeness, and timeliness of the available laboratory and clinical data can be judged only by careful evaluation of laboratory and field staff performance. When available, WHO consultant's reports can serve as useful, independent insights into these problems.

In countries without a national antifilariasis campaign, epidemiological information is more likely to be found in the published literature. The reason for this is that surveys of an investigatory nature are often carried out by academically affiliated or similarly expert research workers. For this and other reasons, survey data tend to be more accurate if less comprehensive than that produced by antifilariasis programs.

Planning a Control Program

There are two possible, though not mutually exclusive, approaches to control: (1) vector control and (2) parasite control through administration of diathylcarbamazine.

Vector control alone, with few exceptions, has proved neither successful nor practical as a control measure. It is costly in personnel and equipment and does nothing to reduce the parasite reservoir. This approach requires that the mosquito population be maintained at a nontransmitting density for 5-10 years or until all existing cases become naturally "burned out." Given the nature of housing, the behavior of the mosquito and its enormous breeding potential in ubiquitous sites, spraying culicine and aedine adults is not a feasible control method. Adulticides are useful only when the sole vector is an anophaline transmitting both malaria and filaria. To be successful in this situation, vector control should:

- be initiated primarily for malaria control;
- be maintained by continual periodic spraying for 10 years;
- be carried out in an island setting or equally "barriered" situation, and finally
- be on guard for insecticide resistance of the vector.

Only in the Solomon Islands were all these factors operative: according to Webber (1977),[20] filariasis virtually disappeared 10 years after initiation of antimalaria spraying operations against A. farauti, A. punctulatus, and A. koliensis-- vectors transmitting both malaria and W. bancrofti.

Antilarval measures against anophaline and aedine vectors have not proved practical. Usually mosquito breeding sites are ubiquitous and cannot be dealt with by the personnel and material resources available in underdeveloped countries. Some Pacific Island countries have attempted antilarval control by educating the people to use "naturalistic" methods, such as emptying coconut husks, covering canoes, etc. It is the author's experience that these educational campaigns have all been failures. Planned "antimosquito week" have been successful, perhaps success extends to the next week, but the ingrained habits and mode of life soon cause reversion to the old "mosquito-breeding" practices. The rigid governmental discipline required to impose effective antimosquito measures can be found in very few countries of the tropical world. Singapore is the exception, though even in Singapore

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mosquito breeding sites created by building excavations in this rapidly developing city-nation are becoming a problem.

Several Asian countries have attempted antilarval control for many years, particulary against C. fatigans. Authorities in these countries admit that control activities are carried on by "inertia." Control activities can reduce the nuisance factor of the vector, but numbers are usually not reduced sufficiently to affect either transmission or filarial prevalence rates. Officials also candidly admit it would be politically inexpedient to disband the sizeable vector control teams. A closed sewage system could reduce or eradicate C. fatigans and B. bancrofti, but this requires enormous capital investment which the poorer countries, whose urban areas are expanding uncontrollably, are unable to finance (or unable to finance in the foreseeable future). Biological control has so far proved ineffective, at least with the techniques available. However, Sasa presents a strong argument for the effectiveness of larvivorous fish and this method should be considered as an adjunctive control method in suitable situations.

In some circumstances, B. malayi can be controlled by destroying the breeding sites when these sites are discreet "Pistia-ponds." This has proved effective in eradicating Malayan filariasis in a focus in Sri Lanka. In most cases, however, the ponds provide food for domestic animals and/or mulch for coconut trees, and the local inhabitants would prefer to live with their filaria rather than live without their ponds.

In old handbooks on malaria control published in India during the 1920s and 1930s, the first page was often devoted to the mosquito net. For decades, the mosquito net was the mainstay of personal antimalarial prophylaxis. With the debut of DDT and the new antimalarials in the late 1940s, the mosquito net lost its virtue as a method of control. Thirty years later, with drug, insecticide and administrative resistance plaguing vector-borne disease control efforts, it may be that the mosquito net's time has come again. The value of the wide mesh net that would allow good ventilation yet protect against C. fatigans has recently been demonstrated by McDonald and Grothans (1973). Widespread use of mosquito nets may be a particularly useful measure where malaria and filaria are transmitted by a common vector as occurs in parts of Indonesia where Anopheles barbirostris carries both infections. Distribution of nets should be considered where the biting activity of the vector and the sleeping pattern of the population coincide.

One difficulty with the net is its misuse. Every entomologist knows that the best way to collect engorged mosquitoes is in the morning inside a faulty net. Bed nets should not be distributed without an accompanying educational campaign on their use and maintenance. Another difficulty is the prevalent view among government officials that the free supply of mosquito nets is somehow immoral: nets are seen as a luxury, not a health necessity. And indeed, nets are a luxury to the abysmally poor of the Third World. However, if proved to be effective, free mosquito nets may be considerably cheaper than the cost of the combined antifilarial-malarial operations which have been so expensive and, too often, ineffective.

For practical purposes, the only effective means to control Bancroftian and Malayan filariasis is by mass drug administration

(MDA) and the only drug available for this is disthylcarbamazine (DEC). DEC comes from the same era which produced the DC-3, and like that remarkable aircraft, it is safe, effective, inexpensive, and dependable. Unlike the DC-3 which has been superceded by swift jets, relatively slow-acting DEC has not been replaced even after 30 years of use.

The success of a MDA antifilariasis campaign depends upon population coverage. Where almost an entire population took the full course, microfilaraemia rates and densities were reduced to the point where little or no transmission occurred. After some years, a dramatic reduction in the clinical rates was also apparent. The critical dosage for Bancroftian filariasis is 72 mg/kg, given in divided doses of 6 mg/kg. The schedule of 12 doses--daily, weekly, or monthly--does not seem to matter as long as the full 72 mg/kg is finally taken. Some programs have used a lower total dosage, 40 mg/kg, for Malayan filariasis, but a growing body of evidence suggests that dosage is inadequate and some experts recommend that 72 mg/kg be given for Malayan filariasis also. Unless coverage and dosage are adequate, any campaign will fail. Therefore, plans for antifilariasis campaigns should include funds to purchase sufficient supplies of DEC, as well as provisions for insuring that population coverage is adequate.

There are two possible approaches to MDA--total or selective population coverage. In total MDA program, everyone (usually over the age of two years) is given DEC while in a selective campaign, only those found positive for microfilaria is pretreatment surveys are treated. The selective approach requires an efficient survey organization, as well as personnel to locate individuals designated for treatment. Total MDA presents difficulties also, particularly in dealing with large populations. The crucial factor is getting compliance from entire communities. Furthermore, a single round of MDA has rarely, if ever, reduced rates and densities to a satisfactory level. In most programs, a second MDA is given 6 months to 2 years after primary administration. The second MDA may aim for total coverage as well or for active case detection with treatment of positives only.

The difficulties in obtaining compliance with drug schedules in public health campaigns are well known. The major cause for drug refusal is the adverse reaction experienced by many microfilarial carriers when given DEC. DEC, per se, is nontoxic; no side effects are produced in noninfected individuals. However, when given to microfilaremic individuals, even if they are clinically asymptomatic, many develop fever, headache, and nausea within several hours of taking the drug. The mechanism(s) which produce the adverse reaction are not well understood nor are there logical, pharmacological measures for blocking them. The problem is now under study: it appears to be an immunologically related phenomenon (Desowitz et al., 1975. Trans. R. Soc. Trop. Med. Hyg. 69:430, research note).

Reactions are generally more severe and commonest in Malayan filariasis than in the Bancroftian type. Because these reactions do occur, careful and convincing health education must be given to the population prior to MDA. They must be told that some will feel ill, but symptoms will be transient and for the patients' good--"The worm is fighting with the medicine"-- and reassured that the

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reaction will not recur, or will be minimal after subsequent dosings. The drug can be given in the evening before people retire so that work loss is minimized. Aspirin and steroids have been shown to be helpful in ameliorating the more severe reactions seen in Malayan filariasis. During the first MDA dose, medical assistance, such as a nurse trained to deal with reactions, should be available.

An important point to consider in planning a MDA antifilariasis program is the method of drug distribution. Most campaigns have employed paramedical personnel for this purpose. In a sense, a MDA is an effort at community participation and serious thought should be given to organizing the community to take on the responsibility of drug distribution. The MDA campaign in Western Samoa was highly successful because of the formation and training of highly motivated village women into health committees which undertook the responsibility for drug distribution. The committee women were real a real "power" group in their community: they knew every man, woman, and child and were able to locate them and insure that each took the full dosage. It is estimated that this approach achieved a remarkable 98% coverage for the first MDA round. The committees had medical supervision and support, but essentially, the campaign was theirs.

If the national health authorities decide that MDA program is not feasible in the foreseeable future, free distribution of DEC, through village dispensary/health stations, should be implemented. In many communities in the endemic zone, there is a growing recognition of filariasis, particularly where the disease is prevalent and a growing willingness to accept self medication. This policy has been adopted in many endemic Indian States, and health authorities there report that it has drastically reduced the incidence and prevalence of clinical filariasis. Over a long period, free distribution of DEC should also reduce transmission.

In 1967, Hawking and Marques demonstrated in a prison population the efficacy of medicating cooking salt with DEC. Several pilot projects since then have confirmed the value of medicated salt in controlling filariasis in closed communities, such as prisons and institutions. In a recent study carried out in India, Rao et al. (1976) showed that medicated salt worked equally well in a village setting when the salt supply was well controlled. With the use of 0.1% (W/W) DEC medicated salt, a 94% reduction in circulating microfilariae was obtained within eight weeks.

Medicated salt appears to be an attractive alternative to MDA by pill. The chief difficulty encountered in the use of medicated salt is limiting all access to any nonmedicated salt. To insure that only medicated salt is available, a government monopoly in salt manufacture is required or, at the very least, a monopoly in distribution of salt manufactured and medicated under terms of strict license. Any prejudices on the part of the population against DEC-salt would have to be taken into consideration.

In summary, a well planned and executed MDA campaign will reduce mf rates and densities within weeks; reduce disease rates within months and years; reduce infection rates in vectors to the point where very low or no transmission takes place.

It will not totally clear microfilaremia from the entire population. Even with complete drug coverage (an ideal, there are always escapees), some individuals remain microfilaremic, usually at much reduced density. A post-treatment survey by 20 to 60 mm^3 thick blood film examination usually shows that about 5% of the formerly microfilaremic group remain positive. The much more sensitive MFC method may demonstrate that the post-treatment residual positivity of this group is perhaps as high as 25% (Desowitz and Southgate, 1973). The epidemiologic significance of this considerable reservoir of "occult" carriers (most are of a density of 1-10 mf/ml) has not been determined. That they are not a danger is evident from the "Samoan experience" which found virtually no transmission had taken place in eight years since a MDA. On the other hand, Bryan and Southgate (1976) demonstrated a concentration phenomenon on the part of the vector since Aedes Polynesiensis became infected after feeding on carriers with 2 mf/ml.

Development of Specific, Measurable Objectives

Ideally, the objective should be the eradication of the disease through interruption of transmission. This ideal can rarely be achieved except in island settings with relatively small populations. In addition, the zoonotic form of B. malayi presents a particularly difficult problem because of other mammalian reservoirs.

The goals for a ten year period can be as follows:

1. Reduction of the total population microfilaremia rate to 1%.
2. Effective treatment of all clinical cases and prevention of further progression of pathology;
3. Prevention of new clinical cases;
4. Interruption of transmission with no new cases after completion of campaign.

The essential data required to implement such a plan include an accurate population census and area maps which indicate all occupied dwellings. Pretreatment blood surveys by 60 mm^3 thick blood films will be needed. A sample of each age group should be processed by MFC of 1 ml of venous blood. The MFC subsample of the 1-10 year group is particularly important because it provides the baseline for later comparison with children born in the 10 years after inception of the campaign. It is these "post campaign" children that will serve as indicators of continued transmission. Very few children have a high enough microfilaremia to be diagnosed by a thick blood film, therefore, MFC is the appropriate technique.

No rigid timetable can be formulated. Each country will have to devise a schedule which will depend on the epidemiological situation, size of population at risk, available staff and funds, etc. The following represents one "ideal" model where the population at risk is sizable but manageable and no budgetary or personnel constraints exist. After the national health authorities have decided to embark on an antifilariasis campaign and have been assured by the government of long-term funding for the program, the following timetable can be applied.

Preparatory Phase, First Year: Appoint program director and four subdirectors, unit chiefs, to be responsible for:
- medical aspects and drug distribution--a physician;
- laboratory services--a parasitologist;
- identification of vectors, elucidation of their bionomics, any

vector control aspects and parasitological surveillance of the vector--an entomologist;
- supplies, vehicles maintenance, budget, etc.--an administrator, "quartermaster."

During the first year, the director and subdirectors acting as a close-knit team will:
- gather and assess all the available information about filariasis in their country;
- plan budgets and staff for their respective units;
- acquire physical facilities (laboratories, offices, etc.) for their units;
- formulate an integrated training program for the units;
- recruit key professional and technical staff and have them receive advanced training where necessary;
- order supplies and equipment for initial surveys and training programs;
- begin formulation of operation timetable and procedures for the National Campaign.

Second Year: Start training laboratory and field personnel. Outside assistance may be needed to establish the first training courses. Health education and "PR" by radio, television, and news media prepare communities for survey. Census team begins mapping dwelling units in first areas designated by timetable. Survey team follows census teams.

The survey team is comprised of three units: blood survey unit for 60 mm^3 thick film samples; "special unit" of well trained venipuncturists to collect samples for subsurvey by MFC: clinical assessment should follow those recommended by the WHO Expert Committee on Filariasis (WHO, 1974). The protocol used will depend on whether the clinical survey is carried out by auxillary medical personnel or medical personnel. Entomological/parasitological survey follows.

Attack Phase, 3rd-5th Years (or longer): Distribution teams give DEC either to total population or to carriers detected by blood survey. Six months after drug distribution, the population/community is resurveyed by 6o mm^{3}blood film and positives retreated with a full course of DEC. Alternatively, a second MDA is given 6 months to 1 year after the first. If the total population is to be covered, the parasitological survey is unnecessary.

Surveillance and Assessment Phase: Surveillance begins when the MDA rounds are completed. Blood surveys can be carried out at 1, 3, and 5 years post-MDA and every 3 to 5 years thereafter. During this period relatively large samples of the population should be examined by MFC. This is particularly important for children born after the end of the MDA campaign since continued transmission can be detected by monitoring this group.

Entomological/parasitological surveillance should also be part of the program. Large numbers of vector mosquitoes will have to be dissected at this time since the infective larva rate will be low. A mass dissection technique with the infective rate expressed as larvae per 100 mosquitoes is useful for post-MDA surveillance (Crans, 1971).

Clinical assessment is more difficult for reasons already noted and requires long term follow-up. Clinical assessment by physicians using the WHO protocol should be carried out post-MDA every 5 years for at least 15 years.

Positive carriers detected by surveys should be retreated. Drug distribution at this time can be integrated into the community health service, e.g., village dispensary/aid post.

Resources: Personnel Resources have already been outlined. Material Resources can be divided into needs for the laboratory and field teams.

Field units will require reliable, sturdy vehicles and a good supply of blood survey equipment, including syringes and needles for MFC collection. These should be the disposable type, but they can be washed, sterilized, and reused if possible.

Laboratory needs include the physical plant. Too often the laboratory of the antifilariasis campaign is relegated to an undersized, poorly lit, and poorly ventilated facility. Such facilities lead to faulty diagnostic work and are costlier in the long run. Microscopists must examine many thousands of slides, a tedious business at best, and should be provided with comfortable surroundings. Purchase of cheap microscopes is false economy. Microscopists should have good quality, binocular microscopes with a good illumination system. Membrane filters (preferably Nucleopore) for MFC are relatively expensive, but the price is much reduced when purchased in bulk. WHO or AID should be approached to purchase large numbers and act as supply agents for regional needs. The usual supply of quality stains (Ciemsa), alcohol, etc., will be needed. The entomological team will need collecting apparatus, dissecting microscopes, etc.

Training programs have to be designed to meet the needs of the professional/technical staff. Funds should be made available early in the program for senior professional staff to visit countries with established filariasis campaigns and training programs. While most countries with antifilariasis programs train their own staffs, some consideration should be given to requesting that WHO establish regional training programs as they did for malaria. Short term courses given by regional and international experts would be highly useful for medical and biological filariasis personnel. The development of such courses, possibly as a "travelling circus," was recommended by the last WHO Expert Committee (1973) but has not, so far, been implemented.

Research on filariasis has languished. A review of NIH extramural grants in this field shows the paucity of research and its general irrelevancy to major problems of the real world. Research on filariasis is best carried out in endemic areas, particularly in those countries with a cadre of trained researchers. Too often these scientists lack equipment and funds for experimental work. They are also often isolated from the mainstream of scientific progress. Collaborative research between national scientists and American and other investigators should be encouraged and supported. WHO Tropical Disease Research Program is now attempting further research on filariasis in endemic zones. It is beyond the scope of this paper to identify research problems in filariasis that should be undertaken. However, it is suggested that an expert group should review these needs and delineate those studies which deserve support.

Integration of Antifilariasis Activities with Other Programs

An antifilariasis control program, if it is of national scope should be a distinct unit with its own budget, personnel, and material resources.

Where no national control program is envisaged, limited antifilariasis activities can be integrated into the health center/dispensary units. The nurse/dispenser can distribute DEC after being trained in dosage schedules and management of adverse reactions. The technician/microscopist, if present at the health facility, can be trained in carrying out parasitological assessment of microfilaremia.

It may also be possible to integrate antimalaria and antifilaria activities since there is some operational similarity, e.g., blood sampling, microscopic diagnosis, population census and surveillance, and in some antimalaria programs, nass drug administration. The integration of these two programs may be particularly feasible where there is a common anopheline vector.

Filariasis should be thought of as a "long term" infection requiring a long-term solution for control. If well organized and population drug compliance is high, the MDA rounds should be completed within 2 to 5 years. The major problem will probably be maintaining surveillance activities for the following 10 to 15 years. Adequate funding for long-term assessment should be developed before an antifilariasis program is initiated. The assessment capability must be kept intact during this long period when vehicles fall into disrepair and space, equipment, personnel, and funds become vulnerable to "raids" by other health programs who consider their needs to be of higher priority.

As in any program whose function depends largely upon long-term laboratory support, difficulties do arise. Microscopists become lax after the examination of many thousands of (mostly negative) blood films over an extended period of time. Supervision and retraining of laboratory staff to assure assessment accuracy is an anticipated problem during the surveillance phase.

Evaluating a Control Program

The parasitologic index (microfilaria rates and densities) is the primary measure of the program's progress. As emphasized elsewhere in this paper, it is essential that parasitologic pre-control data be obtained to provide the baseline against which post-control assessment can be measured. Clinical rates and vector infective rates are other useful indices.

Changes in the health status of a population can be accurately assessed only over a long period of time, probably 10 to 15 years. However, examination of outpatient records in hospitals and dispensaries should indicate if changes in patient numbers and complaints occur and may give early insights into the impact of the campaign upon the health of the population.

Detection of the onset of microfilaremia, by conventional parasitological methods, is a slow process. The onset of disease manifestations is an even more insidious process so the assessment of any campaign will ultimately be based on the long-term follow-up, parasitologically and clinically, of those born after the completion of the attack phase.

In-migration of "carriers" from uncontrolled areas to the controlled areas always presents a problem. Movement of peoples due to social upheaval, as well as national policy for transmigration and resettlement, are particularly important factors in re-introduction of infection.

Ecological changes consequent to human activities may also affect the antifilariasis program and its final resolution. New breeding sites of the vector may be created by rapid urbanization during this period. On the other hand, industrialization and public health engineering works, e.g., building of a closed sewage system, would be beneficial. Fortunately, the main plagues of antimalaria programs, drug and insecticide resistance, have not been documented with antifilariasis MDA campaigns.

At some time during the assessment phase, evaluation should be carried out by an agency independent of the antifilariasis program. As a general principle, it is not sound practice for the organization responsible for "operations" to carry out self-assessment. In large countries with large-scale campaigns involving large numbers of personnel, an independent assessment unit can be established. The assessment unit should be composed of highly trained and well-equipped professional and technical personnel. Their activities should be independent of the operating units and the head of the assessment unit should report directly to the antifilariasis program director or his superior. More modest antifilariasis programs can call upon WHO for short-term consultants to make assessments. In the WHO Western Pacific Region, a filariasis-vector borne disease unit already exists for this kind of advisory purpose.

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MALARIA

by

William Chin

Malaria, more than any other disease, has had the most profound impact on the course of human history. Its effect on a community is vividly described in the following account: "In April 1940, a deadly sickness struck the two villages of Istana Jaja and Pilin in Negri Sembilan. By the time the Institute for Medical Research was notified, much of the damage was done. The padi fields lay untilled and many of the houses were deserted. One grandmother had lost eleven grandchildren. In one house, three adults and two children had died before the house was abandoned. In another, four of the children had died in a month. The disease was malaria." Thus was recorded the experience of uncontrolled malaria in a susceptible community in Malaysia.[1]

From such a picture, it can be seen why malaria has precipitated the fall of nations and even civilizations. Alexander the Great, a world conqueror, succumbed to malaria at the age of 33.[2] His death wrote finis to his dream of fusing East and West into a unified nation, and his empire collapsed. Sir Ronald Rose, who proved that malaria was transmitted by the bite of infected mosquitoes, wrote that "the immense and fertile tract of Africa, what we call the Dark Continent, should be called the Malarious Continent; and for centuries, the successive waves of civilization which have flooded and fertilized Europe and America have broken themselves in vain upon its deadly shores."[2]

Organized malaria control efforts may be divided into three phases: pre-eradication, eradication, and post-eradication. The pre-eradication phase dates from 1897 and Ross' discovery that mosquitoes transmit malaria to the adoption by the 8th World Health Assembly in 1955 of the goal of global malaria eradication. During this period, major control efforts centered on reducing mosquito sources in areas with national socioeconomic importance.

The eradication phase covers the period from 1955 to 1969, when the 22nd World Health Assembly revised its goal from malaria eradication to an acceptance of malaria control as an interim objective. This era was made possible by the discovery of DDT and the subsequent demonstration in temperate zone countries that malaria transmission can be interrupted by spraying house interiors with DDT.

Post-eradication or current control efforts are based on the realization that global malaria eradication cannot be achieved

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through use of a single control method--spraying houses with a residual insecticide. The present period emphasizes flexibility in matching control methods to local epidemiologic conditions and economic realities. The major theoretical differences between the two antimalaria approaches, eradication and control, are summarized in Table 1.

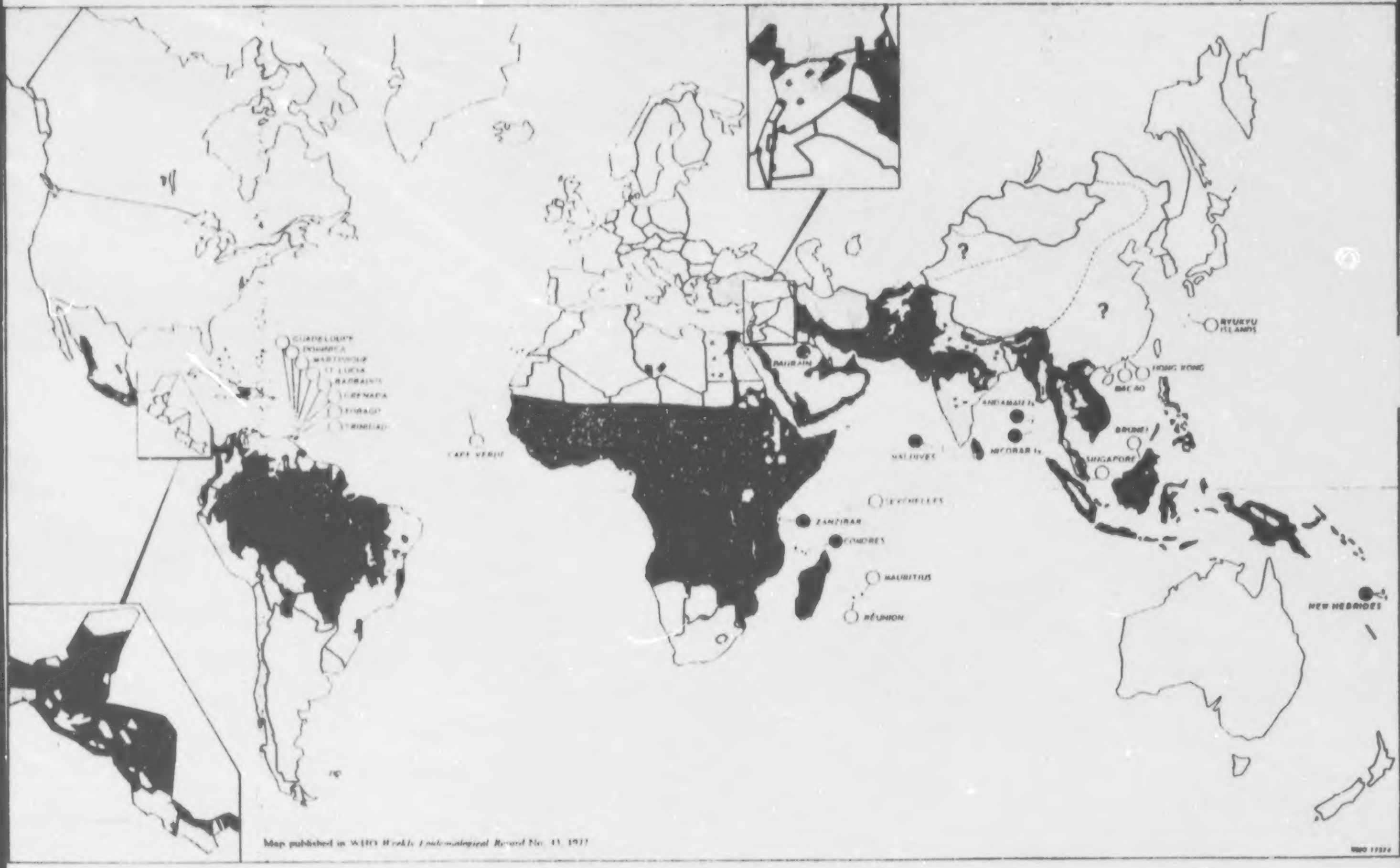
Presently, more than 80 years after Ross' epic discovery and 10 years after the original target date established by the World Health Organization (WHO) for the achievement of malaria eradication, some 1.6 billion people are still at risk for malaria; and 352 million people, mostly in Africa, still live in endemic areas where organized antimalaria efforts have yet to begin. The current global incidence of malaria is estimated by WHO to be 150 million cases with an astonishing 1 million deaths annually in Africa alone. It seems likely that the incidence of malaria will increase in the near future since the disease is experiencing a worldwide resurgence. In countries where malaria eradication projects had achieved significant progress in reducing malaria transmission during the 1960s, severe budget cuts in the majority of programs contributed decisively to the present resurgence. The distribution of malaria as of December, 1976, is shown in Figure 1.

Table 1

DIFFERENCES BETWEEN ERADICATION
AND CONTROL PROGRAMS FOR MALARIA

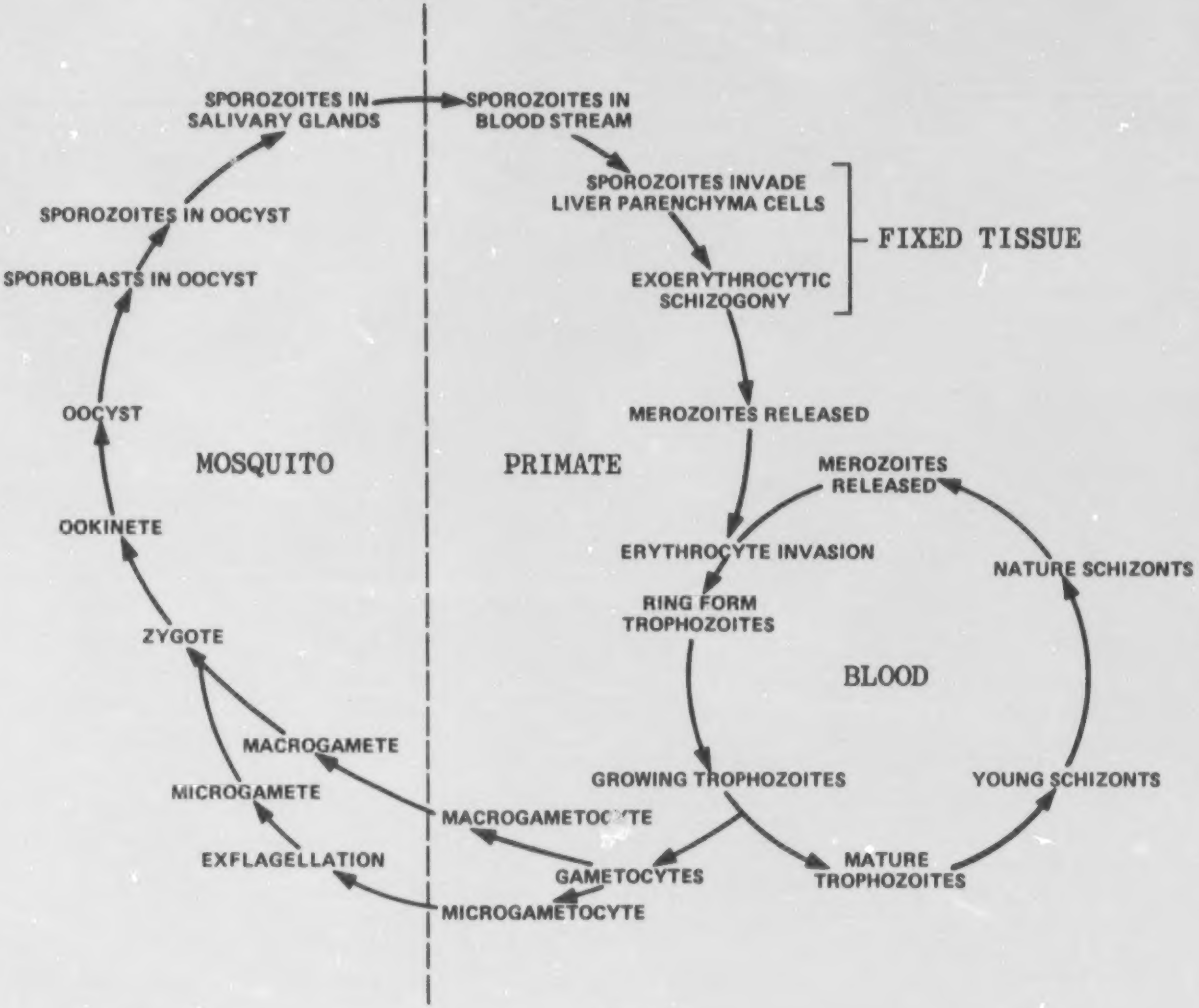
	Eradication Program	Control Program
Objective	End transmission of malaria and eliminate the infective reservoir in man	Reduce mortality and morbidity to lowest level possible
Coverage of Program	All malarious areas	Selective, depending on local resources and feasibility
Duration	Limited to 3-5 years of house spraying with a residual insecticide	No limit
Cost	Large capital investment for limited time	Depends on local resources and allocation for indefinite period
Importance of Surveillance Activities	Primary	Secondary
Efficiency of Program	High efficiency required	Efficiency need not be as high
Optimal Organizational Structure	Autonomous--Vertical	Integrated--horizontal

FIG. I — STATUS OF MALARIA OCCURRENCE, DECEMBER, 1976.


GUADELOUPE
DOMINICA
MARTINIQUE
ST. LUCIA
BARBADOS
GRENADA
TOBAGO
TRINIDAD
CAPE VERDE
BAHRAIN
ANDAMAN Is.
NICOBAR Is.
MALDIVES
SEYCHELLES
ZANZIBAR
COMORES
MAURITIUS
RÉUNION
RYUKYU ISLANDS
HONG KONG
MACAO
BRUNEI
SINGAPORE
NEW HEBRIDES
?
?

Map published in WHO *Weekly Epidemiological Record* No. 43, 1977

Figure 2. LIFE CYCLE OF THE MALARIA PARASITE


SPOROZOITES IN SALIVARY GLANDS
SPOROZOITES IN BLOOD STREAM
SPOROZOITES INVADE LIVER PARENCHYMA CELLS
EXOERYTHROCYTIC SCHIZOGONY
FIXED TISSUE
SPOROZOITES IN OOCYST
SPOROBLASTS IN OOCYST
OOCYST
MOSQUITO
PRIMATE
MEROZOITES RELEASED
MEROZOITES RELEASED
ERYTHROCYTE INVASION
NATURE SCHIZONTS
OOKINETE
RING FORM TROPHOZOITES
BLOOD
ZYGOTE
MACROGAMETE
MICROGAMETE
GROWING TROPHOZOITES
YOUNG SCHIZONTS
MACROGAMETOCYTE
EXFLAGELLATION
GAMETOCYTES
MATURE TROPHOZOITES
MICROGAMETOCYTE

How is it possible in the present space age that malaria still inflicts such a heavy burden of needless illness and death on the peoples of developing countries? The major reason appears to be the abysmal poverty of most developing countries. According to the WHO,[3] no less than 11 countries in Africa expend less than $1 per capita annually for all health activities. The additional fact that African countries have not been recipients or have received only token international assistance, even from the United States Agency for International Development (AID), serves to make the problem more intractable.

Malaria is a focal disease in which the behavioral and ecologic characteristics of the mosquitoes, the parasites, and the human host may differ from locality to locality. Daniels was perhaps the first to recognize the diversity of mosquito breeding sites in Central Africa when he wrote in 1899 that "to a large extent, not only each country but each locality differs in detail."[4] One of the basic flaws of the malaria eradication strategem, therefore, was in ignoring this fundamental principle in the epidemiology of malaria. The assumption that all mosquitoes in malarious areas would respond to the simple attack of spraying house interiors with a residual insecticide assured the failure of malaria eradication efforts.

Malaria in man is caused by four different protozoon species of parasite, each with its own somewhat different pathology and epidemiologic features. The four species of malaria which infect man are Plasmodium falciparum, P. malariae, P. vivax, and P. ovals. While monkey malarias may rarely infect man,[5] such malarias are considered of no epidemiologic significance at the present time.

The life cycle of the malaria parasite begins with the inoculation of sporozoites by bite of an infected female anopheline mosquito. The sporozoites are carried to the liver via the circulatory system where they enter parenchymal cells and begin development into primary tissue schizonts. Depending on the species involved, the time required for these schizonts to mature may range from one to four weeks. This portion of the life cycle is clinically inapparent.

When mature, the tissue schizonts rupture, liberate hundreds of merozoites which invade red blood cells, and initiate the clinical attack. From three to ten days after onset of illness, some of the asexual forms differentiate into sexual forms called gametocytes. The gametocytes have no clinical importance, but they serve as a source of infection for susceptible mosquitoes and, thereby, complete the life cycle. The malaria life cycle is depicted in Figure 2.

It is now believed that some of the sporozoites or intermediate forms of the relapsing malarias (P. vivax and P. ovale) remain dormant in liver cells. At varying intervals which depend on their genetic makeup, some of these latent forms mature into schizonts, release their merozoites, and thereby, initiate a true relapse. The life cycles of Plasmodium falciparum and P. malariae[6] do not produce such dormant forms, and therefore, lack relapse potential. However, asymptomatic infection with P. malariae can persist for more than 40 years.

Ever since Ronald Ross proved that malaria was transmitted by mosquitoes, the vector has been the focal point of eradication or control efforts. Human malaria is transmitted only by anopheline mosquitoes of which there are more than 300 species. Their importance as malaria vectors is determined by certain bionomic characteristics, particularly their feeding habits and their inherent susceptibility to infection with malaria. As an example, the major malaria vector of Central America, Anopheles albimanus, is an inefficient vector because transmission can be maintained only with large populations since this species prefers cattle rather than man for blood meals, and its susceptibility to malaria is low. In contrast, the principal vector in Tropical Africa, A. gambias, prefers man as a source of blood meals, and its susceptibility to infection with malaria is high. Consequently, a much smaller population is required to maintain transmission at high levels.

Examples of important vectors worldwide and their bionomic characteristics are summarized in Table 2.

Depending on the species of malaria parasite, the incubation period usually ranges from 10 to 28 days. At that time, the patient might have experienced headache, anorexia, and malaise of several days' duration and note more recent symptoms of nausea, vomiting, myalgia, and fever with or without chills.

Paroxysms of fever are synchronous with the completion of each asexual cycle: They occur every 42 to 48 hours in pure single-brood vivax, 50 hours in ovale, 72 hours in malariae, and approximately 48 hours in falciparum infections. The pyrexial attacks are usually characterized by three stages: (1) a cold stage ranging from a sensation of chilliness to uncontrollable shaking which ordinarily lasts for 15 minutes to 1 hour, (2) a hot stage of fever, and (3) a sweating stage characterized by profuse sweating.

Various symptoms and clinical signs that often occur with faciparum infections are rarely, if ever, seen in other malarias. These manifestations (shock, renal failure, acute encephalitis, and coma) are directly related to the involvement of one or more organ systems by falciparum parasites. These complications or malignant forms occur in falciparum malaria and are absent in the other malarias because the falciparum parasite accomplishes the major part of its development in the deeper circulation of organ systems. In contrast, vivax, malariae, and ovale parasites accomplish their entire development in the peripheral circulation. Additionally, there is a tendency for vessel membranes to react to the stimulus of falciparum parasites by an inflammatory reaction which results in the escape across the endothelial membrane of water and large molecules, especially protein. The end result is compromised circulation to vital organs due to stasis caused by the adherence of parasitized red cells to vessel walls and to one another.

Individuals with vivax, ovale, and malariae infections usually recover, even without antimalarial therapy, provided they do not develop complications with other infections or conditions. Recovery is due in part to a degree of acquired immunity, whereby, parasitemia is kept at a fairly low or safe level which is rarely greater than 50,000 parasites per cu. mm. of blood. With falciparum malaria, however, the degree of acquired immunity for some reason is delayed since parasite counts usually continue to rise in the absence of treatment. A parasite count of 500,000 per cu. mm. of blood for falcimparum malaria indicates a very grave prognosis.

Table 2

MAJOR VECTORS OF HUMAN MALARIA

Species	Distribution	Susceptibility to Malaria	Host Preference	Typical Breeding Sites
A. albimanus	W. Hemisphere from S.E. Texas, Mexico, Central America to Ecuador--Colombia--Venezuela and West Indies	Slight	Animal	Wide Range from temp. rain collections to ponds, streams and lakes
A. darlingi	S. America east of the Andes to Argentina	Moderate	Man	Clear, fresh shaded or partially shaded waters, lagoons or marshes
A. gambiae	Tropical Africa	High	Man	Any fresh water collection exposed to sunlight
A. culicifacies	Indian Subcontinent	Slight	Animal	Sunlit collection of fresh water including rice fields
A. minimus	S.E. Asia	Moderate	Man	Margins of slow moving sunlit streams
A. maculatus	Foothills of S.E. Asia countries and Indian Subcontinent	Moderate	Animal	Sunlit hilly streams
A. balabacensis	Jungles of S.E. Asia	High	Man	Any densely shaded water collection
A. stephensi	Urban areas of Indian Subcontinent and Middle East	Moderate	Man	Shaded wells, cisterns, cans, roof gutters

In general, the death rate for falciparum malaria is directly proportional to the interval between onset of illness and the time that diagnosis is made and/or antimalarial therapy is administered. It is these falciparum infections which extract such high mortality in infants and children in Tropical Africa.

Treatment of Malaria

The treatment of malaria in a semi-immune population is relatively simple. A single oral dose of chloroquine of 10 mg/kg will cure clinical attacks due to all four species of malaria. The only exception is chloroquine-resistant falciparum malaria. Resistant strains, at present, are highly prevalent in Southeast Asian countries from India to New Guinea. They are also found in South America and extend north Panama. To date, chloroquine-resistant falciparum malaria has not been documented in the Middle East, Central America (aside from Panama), or Africa. Two cases of chloroquine resistant falcimparum malaria, acquired in Africa, have been detected recently. Both patients, one from Denmark and the other from the U.S., acquired their infections in the Mombasa area of Kenya. These resistant strains are commonly treated with quinine alone or in combination with pyrimethamine and sulfonamides.

Primaquine is another antimalaria drug which is useful for the prevention of relapses due to infections with vivax or ovale malarias and for the eradication of falciparum gametocytes to prevent further infection of mosquitoes. Some caution has to be taken when using primaquine in population groups with G6PD deficiency, since the use of primaquine in individuals with this enzyme deficiency can result in hemolysis.

Man is susceptible to all four species of human malaria with one notable exception--most Blacks are not susceptible to infection with vivax malaria. The relationship of this insusceptibility to the absence of a Duffy blood factor has been demonstrated recently by Miller et al.[7] Serologic surveys conducted recently in Tropical Africa indicate that the population prevalence rate of Duffy negative phenotype is about 90% and, thus, provides a firm basis for the observation that vivax malaria is not found in West Africa.

Certain hemoglobinopathies confer a degree of protection against falciparum malaria: this has been demonstrated convincingly in the case of sickle cell heterozygates. While the evidence is not nearly as clear cut, protection from falciparum malaria in carriers of B-thalassaemia and hemoglobin E has also been observed. This protection is manifested by a significantly lower density of falciparum parasites.

Immunity to malaria, unlike most viral infections, is acquired slowly and only after repeated exposure to the parasites. The fact that immunity against malaria, found in most African adults, becomes functional only after years of repeated infections and at a considerable cost of high mortality in infants and children under five needs to be stressed. Infants and children are not only predisposed to higher rates of morbidity and mortality through lack of immunity, but they also provide a greater source of malaria parasites to biting mosquitoes. Pregnant women are another group at special risk to malaria. In a study reported by Gilles et al.[8] from Nigeria, attacks of clinical malaria were 4-12 times more frequent in a group of pregnant women than in those not pregnant. The results suggest that there is a decrease in host immune response to infection with malaria during pregnancy. The reason for this observed decrease in immune response is presently not known.

Classification of malarious areas is accomplished by two major methods: quantitative--by the degree of endemicity, and qualitative--by the stability of malaria transmission.

Endemicity refers to the degree of natural malaria transmission within a community. Implicit in a definition of endemicity is the ability to measure incidence, the number of cases of malaria in a known population over a unit time; or prevalence, the number of cases in a known population at any given time. The most frequently used classification of endemicity was adopted at the 1950 WHO conference in Kampala. In this system, the rate of spleen enlargement in children 2-9 years old is used as the measuring unit. Thus, endemicity was classified as follows:

- Hypoendemic: spleen rate of 0-10%.
- Mesoendemic: spleen rate between 11-50%.
- Hyperendemic: spleen rate in 2-9 year olds constantly greater than 50% coupled with a high spleen rate in adults.
- Holoendemic: spleen rate in 2-9 year olds constantly greater than 75% coupled with a low spleen rate in adults.

This classification scheme was found useful in Tropical Africa, but attempts to use it in other areas where the dynamics of transmission and the predominant species differed produced inconsistent results. Dissatisfaction with spleen enlargement rate as a measurement of endemicity among malariologists led to a proposal in 1959 by Metselaar and Van Thiel[9] to replace spleen enlargement rate with parasite rate in children aged 2-9 years.

Neither is satisfactory for present use by developing countries that plan to undertake malaria control programs. Spleen enlargement surveys have become a lost art; but more importantly, the frequent use of available antimalarials in endemic areas probably modifies malaria infection, and, thereby, significantly lessens the response of the spleen to malaria infection. While parasite rates may be more useful as a measure of malaria endemicity, such rates are obtainable only if laboratory facilities are available. Further, the reliability of such rates depends not only on the competence of the microscopists but also on the efficiency of case detection efforts.

For the future, serologic tests to detect the presence of malarial antibodies may be the method of choice. The serologic tests currently available--the indirect fluorescent antibody test (IFA) and the indirect hemagglutination test (IHA)--are also incapable of meeting the needs of malariometry in developing countries due to the highly technical nature of the tests which require laboratory personnel with a great deal of experience. A second generation of serologic tests, principally the Enzyme Linked Immunosorbent Assay test (ELISA) currently under development at several laboratories, including the Center for Disease Control, Atlanta, has high potential for standardization and automation, requirements necessary for operational use in malarious areas.

The concept of stable or unstable malaria transmission was first proposed by Macdonald[10] and rests on the efficacy of the local anophelines as malaria vectors. In much of Central America, for example, the vector, A. albimanus, tends to feed on cattle and the presence of breeding sites is highly dependent on availability of water during rainy seasons. The probability is not high that a given mosquito will first bite a gametocyte carrier, survive for 12 days, and then bite a susceptible host--particularly during the dry season. Under such circumstances, malaria transmission is considered unstable since optimal conditions are required to produce the high vector density necessary to maintain transmission. In areas of stable malaria, found in most of Tropical Africa, the high efficiency of the vector, such as A. gambiae combined with its natural preference for human blood meal, enables intense malaria transmission even when climatic conditions are far from ideal. In endemic areas with unstable types of transmission, control of malaria can be accomplished far easier than in stable areas.

Estimate of the Current Problem

In Africa the vast majority of the malarious areas, particularly south of the Sahara, are still without comprehensive malaria programs. It is estimated that of 248 million persons at risk, only 6.5% live in areas which are engaged in activities such as mosquito control efforts and limited periodic mass distribution of antimalarials to segments of the population at special risk. The areas covered are mostly large towns, international seaports, and airports.

While accurate data on endemicity are unavailable, periodic smear surveys in many of the African countries have resulted in a rather wide range of positive smear rates, from 24% to 76%. More reliable, perhaps, are survey findings that consistently showed a predominance of falciparum malaria, which accounted on the average for 87% of all malarias.

In Latin America the malaria picture in most of the 21 countries has either been stabilized or improved. Some exceptional situations exist, such as the notable resurgence of malaria in El Salvador, Honduras, and Nicaragua, which reported 83,290; 48,749; and 26,228 cases in 1976 respectively. More recently, an increase in malaria transmission in Peru and Guatemala has been reported. In problem areas of Latin America that comprise approximately 20% of the population, the major technical obstacle which has impeded progress in malaria control is the presence of vectors resistant to available insecticides.

On the Indian subcontinent the severity of the malaria problem in India, Bangladesh, Pakistan, Nepal, and Sri Lanka, is second only to that found in Africa. In recent years, the resurgence of malaria occurred with such fierceness it overwhelmed the surveillance systems in most of these countries and resulted in totals of recorded cases which are but a minor fraction of the actual number of infections transmitted. Estimates from various sources, including local health authorities, WHO, and AID, indicate that total malaria cases in this region exceeded 10 million for 1976: India and Pakistan alone accounted for approximately 8 million.

It is considered highly probable that malaria transmission will continue to increase in the near future due to unresolved administrative and budgetary problems as well as the inability of local malaria programs to successfully negotiate the transition, both conceptually and operationally, from eradication to control. Compounding these problems is the apparent westward spread of chloroquine-resistant falciparum malaria. Presently, such strains have been reported from Assam, India, and Bangladesh. Resistant infections reported from Nepal were probably acquired in India.

The Southeast Asia and Western Pacific region extends from Burma on the west to Indonesia in the east. Little reliable information is available from Laos, Cambodia, and Vietnam--an area inhabited by approximately 58 million people. The Philippines and Malaysia continue to show slow but steady progress toward malaria control. The malaria problem in Burma, Thailand, and Indonesia is deteriorating. In Burma, malaria, at present, is the communicable disease with the highest incidence. Thailand reported 90,000 cases in 1972. Based on the author's visit to that country in February, 1977, the case rate for 1976 was estimated to be at least 10 times that of 1972. Indonesia, with a loan from AID, is currently engaged in an intensive antimalaria campaign which has so far succeeded in reversing an upward trend in malaria incidence in Java and Bali. In 1973, the number of cases detected in these islands were 346,233; but in 1976, only 96,999 cases were identified.

Eastern Mediterranean reports show that in the southeast part of Turkey, malaria transmission reached epidemic proportions in 1973 when 37,321 cases were reported from that country. Currently, the incidence of malaria in Turkey continues to increase. Of the other countries of this region, Jordan, Libya, and Tunisia continued to report satisfactory progress while Iran, Iraq, and Syria reported renewal of transmission in previously malaria free foci. Malaria transmitted in these new foci contributed significantly to the total of 47,653 cases reported from Iran in 1976.

Existing sources of data for all regions include:

- Surveillance Operations--usually found in countries with established malaria programs.
- Periodic Smear Surveys--usually made in countries without organized malaria programs such as most of the African countries. These surveys are generally conducted or supervised by WHO personnel.
- Other--additional data may originate from other external groups in the course of field research on malaria or other medical problems. The most current malaria data available were compiled by WHO.[11]

The global malaria control situation for 1976 was summarized as follows:

Area	Population (in millions)
Originally malarious, Total	2,048 (100%)
Malaria reported as eradicated	436 (21%)
Engaged in malaria control activities	1,260 (62%)
With no malaria control activities	352 (17%)

The present global resurgence of malaria has prompted international agencies, notably WHO and AID, to intensify their technical and financial support of malaria programs in developing countries. Still more important, it has made developing countries realize that, despite their meager resources, the malaria problem can no longer be ignored. The following are actions being taken in an

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attempt to reverse the presently deteriorating malaria situation:

A major government in Tropical Africa, Nigeria, has for the first time declared its commitment to control malaria by undertaking a countrywide antimalaria campaign.

The government of India will increase its malaria control budget to approximately five times the budget of 1973-74 and has redirected antimalaria efforts. The highest priority has been assigned to the prevention of mortality by providing antimalarials free to all suspected cases.

The AID has increased its support of the antimalaria effort by providing more funds for malaria research (mainly for vaccine development). But lower level of support is provided for research on the development of new insecticides and alternative methods of mosquito control. In addition, the Agency is granting substantial loans to Pakistan, Indonesia, and Sri Lanka to assist the malaria control programs of these countries. Finally, grant funding to the malaria programs of Nepal and Haiti is being continued.

The realization that malaria control, unlike eradication, has no time limit and must be operated within existent financial and human resources has led to major changes in the organization of malaria programs. The community is now considered a resource in the planning and implementation of malaria control programs. Recognition that the community played a vital role in eradicating malaria from Cuba and that community members, who act as voluntary collaborators in most Latin American countries, detect and treat a majority of their malaria cases, has prompted this new view among national authorities.

Countries with experience in malaria eradication programs are also converting once autonomous, vertical operations into horizontal structures by merging malaria activities with basic health services. Countries without the precedence of previous malaria programs are organizing "integrated" programs. Due to poor planning and implementation, mergers of malaria activities with basic health services have proved less than successful in most instances and disasterous in some. For integration to succeed, it will be necessary to proceed cautiously and slowly with careful timing to ensure that integration does not take place until endemicity has been reduced to a level which an integrated service can manage.

Evaluation of Existing Programs and Research

In the ten years from 1956-1966 when global malaria eradication activities reached their zenith, all eradication programs functioned autonomously. The program director exerted absolute control over a vertically organized structure and directed activities from a central headquarters through successively lower units to the field. It was recognized in the late 1960s that the goal of malaria eradication was no longer tenable for the near future because of administrative, financial, and technical problems. This conclusion was made official in 1969 by the 22nd World Health Assembly which revised its goal of malaria eradication to the acceptance of malaria control as an interim objective. WHO took the lead in implementing the control strategy by reorganizing its headquarters staff and changing the name of the Division of Malaria Eradication to the Division of Malaria and Other Parasitic diseases. The WHO action was followed by conversion of many Malaria Eradication Programs to control programs, in name at least.

The major problems which arose from attempts by eradication programs to convert to control programs have remained mostly unresolved in the nearly ten years which have elapsed. For example, lack of trained malariologists is a basic problem. In a control program without simple guidelines, precise goals, or recent examples to emulate, efficient operation requires that each program have trained malariologists to evaluate problems and select control measures suited to local conditions and economic realities. Unfortunately, such professionals are extremely scarce at the present time. These personnel were the first casualties of the eradication era: they were displaced in many instances by operational and managerial specialists.

Administrative and personnel problems continue. Problems that arise from the integration of a once highly elite organization whose staff became accustomed to special privileges--bonuses for field work, rapid promotion, and regular use of official vehicles--to a subordinate role within the basic health service are especially difficult to resolve.

Formulation of policy for malaria control by individuals without malaria experience causes problems. Policy makers for the integrated Basic Health Service may not view the malaria problem with the same sense of urgency. Thus, in 1974, at a time when malaria transmission reached epidemic proportions in Pakistan, the Secretary of Health from one province stated that he considered malaria to only have third priority, after Maternal and Child Health and Population Control.

In planning for staffing and training program personnel, a basic consideration is the training required by senior staff members. Plans for staffing and training should include the commitment to undertake a control program of indefinite duration. There is no need, then, for hasty decisions which are often associated with "crash programs."

In a control program, the medical officers in charge of the program at various levels will need to know not only the basics of malariology but must also be well trained in other aspects of preventive medicine. Thus, long-term training with emphasis on career development should be promoted. Since decisions about control measures should be made locally to suit local conditions, the training given such medical officers must include a systematic approach to data analysis; the logical selection of control measures to meet specific problems; and finally, the evaluation of control program accomplishments.

With technical assistance from international groups, schools of public health in developing countries should be strengthened by upgrading specific training programs in disease control. The curriculum for training in malaria control should be revised, with outside consultation, to reflect local epidemiologic conditions and socioeconomic realities. Separate curriculum should be developed for medical officers and non-medical officers, such as entomologists, parasitologists, and engineers. Currently, training that leads to a M.P.H. degree is available from the Schools of Public Health in Teheran (English) and Mexico City (Spanish).

Malaria control is an ever-evolving concept: no standard manual exists to guide every aspect of control operations. Therefore, an important program component must be the utilization of innovative methods in conjunction with continuous evaluation of the results obtained. Medical officers should be provided the opportunity to gain practical research experience either as part of a M.P.H. course or as a trainee assigned to established malaria research centers. When training is completed, a close relationship should exist between trainee and teachers. The research centers should be available for advice on a continuing basis.

Surveillance operations comprise data gathering to monitor the status of malaria transmission. Primarily, these activities include case detection and evaluation of the mosquito vectors, particularly their response to insecticides.

Generally speaking, no single method of case detection is adequate to produce results which give a precise picture of malaria endemicity. The reliability of case detection data depends on the competence of the microscopists; yet high error rates in smear diagnosis by "experienced" microscopists are not uncommon. Perhaps of greater influence on the reliability of endemicity data is the efficiency of the various case detection methods.

Active Case Detection (ACD) includes house-to-house visits by a malaria worker on a regular schedule, usually once a month. Blood smears are taken from occupants who report fever at any time since the last visit and a single dose of antimalarial is given.

Passive Case Detection (PCD) establishes malaria detection posts in Medical and non-medical facilities. In the latter case, the post is usually staffed by a voluntary collaborator. Local residents who suspect their illness may be due to malaria attend these posts to receive treatment and may provide a drop of blood for a smear. Activated Passive Case Detection (APCD) simply refers to a PCD post staffed by a malaria worker.

Mass blood surveys provide blood smears taken from as many individuals in a community as possible. Such surveys are usually undertaken in areas of unusual malaria outbreaks in an attempt to identify as many of the cases as possible.

Malariometric surveys are carried out among selected age-groups usually in children with a sample size that is approximately 10% of the group. While the usual survey method is to take blood smears, a malariometric survey particularly before the malaria eradication era might have consisted of only a spleen survey. Malariometric surveys are the least sensitive and have been used traditionally in pre-eradication evaluations to provide a crude estimate of malaria endemicity.

Serologic surveys require sophisticated equipment and well-trained staff which are not readily available in developing countries. Serologic tests include the Indirect Fluorescent Antibody Test (IFA), which has the advantage of sensitivity but lacks the potential for mass use; the Indirect Hemagglutination Test (IHA), which lacks the sensitivity of the IFA, but thousands of samples may be performed per day by an experienced laboratory; and the Enzyme Linked Immunosorbent Assay Test (ELISA). This is the most recently developed serologic test. It has yet to be completely evaluated, but results to date indicate a high potential for standardization and automation, both necessary for operational use in the field. It should be emphasized that all the serologic tests measure the presence of malaria antibodies and cannot distinguish between current, recent, or past infections.

Entomologic monitoring is an important part of a surveillance system. Entomologic information can be gathered only by well-supervised, thoroughly trained entomologists and their assistants. Personnel of this type, like the malariologists, are also few in number. The purposes of entomologic monitoring are:

- to identify any species and determine the relative proportion and habits of local anophelines.
- to determine the susceptibility of local anophelines to malaria infection.
- to determine the degree and intimacy of contacts between man and vector.
- to determine the susceptibility of the local vector to insecticides.

A major mistake of the eradication era was the decision of the funding agencies to deemphasize research: it was thought that additional knowledge of malaria was not required to successfully execute the eradication program. Thus, during the 22 years (1950-1972) of AID's financial support to malaria programs around the globe, only 0.1% of the $1.2 billion total was allocated to research. Until 1966, the bulk of this research fund was spent on improving and monitoring formulations of insecticides and on evaluating the hardware required to apply them. Since 1966, the emphasis has been changed to support of operational research on the major technical problems that impede progress in malaria eradication. The scientific community, on the other hand, did not abandon malaria research during the decades of malaria eradication. On the contrary, the urgent need to protect and treat U.S. military personnel in Vietnam who acquired chloroquine-resistant falciparum malaria greatly stimulated the U.S. Army's search for more effective antimalarials. The academic community and traditional malaria research groups in Great Britain and the U.S. Public Health Service pursued studies and contributed greatly to our present knowledge of malaria immunology. Important work was also accomplished on serologic tests for human and non-human malaria, and on the basic biology of malaria in monkeys and other animals.

Presently, stimulated by the global resurgence of malaria and promoted by the WHO special program for Tropical Disease Research, there are high hopes that practical malaria research directed toward the many technical, administrative, and human problems that confront malaria control programs may finally be supported. So far, action to implement such research is moving at an excruciatingly slow pace. The major reason again is the lack of trained personnel who have the experience to formulate and undertake meaningful research, particularly in the developing countries.

Assisted by significant funding from AID, immunologic studies directed toward vaccine development are assigned the highest research priority. It may be many years before a final product, if any, is available. No one knows that better than the Director General of WHO who stated in 1975: "There are no miracle technical solutions to the problem (of malaria) and there is no prospect of such solutions being developed and becoming available for wide application for a number of years to come."[12]

Despite general pessimism about the feasibility of developing a malaria vaccine for mass use in man, a mood shared by many knowledgeable malariologists, little doubt exists that due to the stimulus of AID funding, significant progress has been reported in recent years. This includes:

- immunization of mice with irradiated sporozoites of P. berghai conferred absolute immunity to subsequent challenges.[13]
- immunization of man with irradiated sporozoites of P. falciparum conferred absolute immunity for three months.[14]
- Rhesus monkeys may be protected from P. knowlasi infection following immunization with merozoites of P. knowlesi combined with Freund's complete adjuvant.[15]
- chickens immunized with irradiated P. gallinaceum gametes produced antibodies which had a decided inhibitory effect on the gametocytes ability to infect mosquitoes.[16]
- Trager and Jansen of the Rockefeller University developed a method for the continuous cultivation of falciparum malaria.[17]

In chemotherapy, the screening of more than 200,000 compounds by the U.S. Army Antimalarial Drug Development Program led to identification of a handful of highly promising drugs for testing in man. Of these, one of the more promising is mafloquine, a 4-quinoline-methanol, which when given in a single oral dose has already demonstrated high efficacy against P. vivax as well as drug sensitive and drug resistant P. falcimpaum malaria.[18] Studies on newly synthesized insecticides and on the biologic control of the malaria vector are also being pursued.

Present research activities that emphasize the operational aspects of epidemiology and control methods are notably scant. A better balance between basic research and operational research is urgently needed. Listed below are suggested studies which fall into the general category of "practical malariology."

Development of Better Assessment and Control Methods:

- Develop a systematic approach for the delineation of non-malarious from malarious areas and the stratification of malarious areas by endemicity and national socioeconomic importance. Different types of survey methods need to be evaluated to determine accuracy, simplicity, and lowest cost.
- Evaluate various devices for trapping mosquito vectors to maximize the reliability of vector density estimates.
- Develop and evaluate methods for continuous assessment of malaria control activities that are more reliable and cost effective than the present ACD system.
- Develop and evaluate methods for early detection and response in malaria epidemics.
- In collaboration with agencies having access to computerized library search, develop bibliographies on pre-DDT malaria control methods.
- In areas with large but restricted breeding sites, evaluate mosquito control through larvivorous fishes.
- Evaluate community participation projects which include use of the following elements: voluntary collaborators, pyrethrum spray, mosquito nets.
- Develop national awareness of the malaria problem by teaching students, health planners, government employees, and the average citizen. Teaching methods which have the greatest impact on each of these groups need to be developed and evaluated.

Studies of the Effectiveness of Drug Therapy:

- Undertake studies of vivax malaria curative therapy in order to develop the shortest treatment course with the highest cure rate.
- Perform surveys to delineate the distribution of chloroquine-resistant falciparum malaria.
- Develop methods to minimize the spread of chloroquine strains of falciparum malaria.
- Contract with academic institutions to develop competence in the in-vitro testing of the response of local falciparum strains to standard antimalarials.

With few exceptions, all of the studies outlined above should be performed in countries confronted with malaria problems. Experienced investigators must fill dual roles of researcher and teacher. Local health and academic personnel must be completely involved in research from the draft of the research protocol through implementation and analysis of the results.

No better evidence is needed that the majority of developing countries are failing to cope with the malaria problem than its continuing increase. The two major factors responsible for the present state of affairs are:

(1) Many developing countries have no comprehensive program of malaria control due to lack of sufficient resources and a multitude of competing problems.

(2) In countries with organized programs, the present period of transition from eradication to control has been characterized by confusion and continuing debate over strategy. The result is indecisive or ineffectual action in many national programs and inaction in others.

The prospect for improvement in the near future does not appear bright. For many countries to begin a comprehensive malaria control program and for others to improve the efficacy of existing programs, external technical and financial assistance will be required.

Planning a Control Program

Program objectives listed in order of possible attainment from least difficult to most difficult are as follows:

1. Elimination of mortality due to malaria.
2. Reduction of excess morbidity due to malaria.
3. Reduction of malaria transmission in areas of national socio-economic importance (e g., cities, transmigration developments, etc.) to a point where it is no longer a public health problem (below an incidence of 1 case/1,000 population/year).
4. Reduction of malaria transmission in other areas to an incidence level below 10 cases/1,000 population/year. For much of Tropical Africa, a reduction in malaria transmission to a level below 100/1,000 population/year would be a major accomplishment.
5. Interruption of transmission which leads to eradication.
6. Maintenance of eradication through development of a sensitive method of surveillance and a system of prompt response to renewal of transmission.

Control methods include measures aimed at reducing both vector population and disease reservoir. Residual spraying of house interiors with insecticides, as demonstrated during the eradication era is still the most effective method in areas where vectors rest indoors long enough to absorb a lethal dose of insecticide. Unfortunately, this method is the most costly due to rising insecticide costs. Another problem which has worsened since the eradication era is the development of vector resistance to DDT in many parts of the world. In some countries, such as Pakistan, those areas where DDT is still effective represent only a minor part of the malarious areas. The need for alternative insecticides, such as malathion, not only increases operational costs considerably but may pose serious hazards for handlers if they are not well trained.[19]

Outdoor application of insecticides, such as malathion or synergized pyrethrins, may be made by aircraft or big ground equipment mounted on vehicles or carried as backpacks. Its chief value is in combating epidemics of mosquito-borne disease in areas of population concentration. Outdoor spraying has little or no residual effect and must be applied repeatedly. However, the equipment and insecticides are too expensive for routine application.

Other control measures aimed at vector population include biological control by the use of larvivorous fishes; application of safe larvicides; and reduction of mosquito breeding sites by drainage.

Measures aimed at reducing the disease reservoir (human infections) include the use of antimalarial drugs to treat malaria cases in a given area. Another chemotherapeutic method used to combat malaria is mass drug treatment of entire populations or groups at special risk. The antimalarial, usually chloroquine, may be administered at scheduled intervals, usually once a week up to once a month, or continuously in the form of medicated salt.[20] For either schedule, the problem which has generally rendered mass chemotherapy ineffective is the reluctance of a significant proportion of the population to cooperate, especially when such methods are carried out over an extended period of time.

Community and personal participation in malaria control is important. In devising a strategy for malaria control in developing countries, one must distinguish between countries confronted with the problem of converting an eradication program to one of control and countries where organized antimalaria programs never existed. The latter countries have a population currently of approximately 352 million people and spend an average of $1 per person per year for all health activities. Dr. Paul Russell's advice given 40 years ago should be recalled when considering malaria control methods to be used in these nations. Dr. Russell noted, "In the rural tropics, time has far less importance than money. Cheapness, not speed is essential. Further, persistence, not perfection, should be the motto." Plans for new programs should be guided by this principle. Project proposals calling for expenditures of millions of dollars are clearly unrealistic.

With few exceptions, one type of control program which has not been given serious consideration is community and personal participation in antimalaria efforts. For countries with no history of organized antimalaria efforts and a rural health infrastructure which is minimal or non-existent, malaria control programs based primarily on self-help projects in local communities should be considered.

The basic difficulty in a discussion of community participation in malaria control efforts is the simple lack of standards by which such projects may be judged. With rare exceptions, such efforts have either not been attempted; or if attempted, not well organized, supported, and sustained. Drawn from the collective experience with Latin American malaria programs by CDC staff in the Bureau of Tropical Diseases, the following guidelines are offered for consideration.

For any self-help project to become operational, it requires the organization and support of well-trained professionals. Such projects must be an integral part of a comprehensive program operated by a central authority. Steps in the organization of community participation projects for malaria control include:

a. Assess the local problem in terms of vector breeding sources, mortality, morbidity, and infection rates.
b. Determine the knowledge and attitudes of the community about malaria.
c. Inventory local resources, including manpower, skills, schools, dispensaries, and public meeting places.
d. Select, with professional guidance, appropriate measures for community involvement.
e. Discuss, with community leaders and with community members, implementation of the program.
f. Initiate plans for implementing the program and develop health education approaches for population segments involved.
g. Provide continuing support, backup services, and evaluation.

Methods of community participation differ. In areas where breeding sites of malaria vectors are ubiquitous, as is the case with A. gambiae in Africa and A. balabacensis in the Far East, utilization of methods to reduce larval development would not be feasible. In other areas, particularly in malarious villages in Tropical America, malaria is transmitted by anophelines that breed in relatively restricted sources within the confines of or in close proximity to the village. In many instances, such sources can be reduced or even eliminated by the use of the following methods applied singly or in varying combinations:

Drainage or stream redirection procedures can be carried out by locally available labor working with hand tools under the direction of community authorities and/or personnel of the central malaria control organization. In situations where larval habitats encompass large areas, initial source reduction may require heavy equipment and operators. In such a case, active collaboration with the public works agency may be required.

Larvivorous fish, such as Gambusia and other guppy types, have been used successfully by various malaria programs to control mosquito larvae. If the use of such a method is contemplated, it will be necessary for personnel of the malaria program to select the appropriate species of fish (preferably indigenous to the local area), establish hatcheries, and instruct the community in the periodic transfer of the fish to mosquito breeding sites.

Larviciding is a traditional method for the control of mosquito larvae. In breeding sites where the water is not ordinarily used by the villagers, such as in marshes or pasture, used motor oil remains a useful and economical larvicide. In situations where water is used by the villagers, consideration should be given to the use of safe larvicides, such as Abate or Altosid (a growth regulator) absorbed onto sand or ground corn cobs. The advantages of the use of such formulated larvicides are the ease with which they can be applied by hand broadcasting and the relatively long duration of action due to slow release of the larvicide from the sand or other granular carriers.

The idea of utilizing non-salaried, volunteer collaborators to assist malaria programs in dispensing antimalarials originated in Latin America. As early as 1937, the malaria program in Venezuela had organized treatment centers in postal or telegraph offices and schools where quinine was made available to fever cases. Presently, in most Latin American malaria programs, the volunteer collaborators play an important role in malaria treatment and case detection. Recent data from the malaria program of El Salvador, Central America, indicate that volunteer collaborators did more than any other antimalarial effort to achieve the virtual elimination of malaria mortality.

The volunteer collaborator system has been an efficient and economical method for malaria detection and treatment in most Latin American programs. Many other malaria programs have not taken advantage of the volunteer collaborator system. The reason most often cited is that such posts require staffing by malaria or other health personnel: it is felt that lay persons, due to lack of background and training, are incapable of assuming responsibilities for dispensing antimalarials and taking blood smears. The results of the system in Latin American countries have convincingly demonstrated that educational level or previous experience in health related fields plays no role in determining the performance of volunteer collaborators. If the sole function of the collaborator is to dispense antimalarials, the only requirements are the individual's willingness to serve and the ease of access to the treatment post. If case detection is also to be a duty of the collaborator, then the ability to read and write is essential.

The system of volunteer collaborators has potential to serve other community health needs. With experience and slow, deliberate, step-by-step training, the following additional duties may be added:

- Disseminate information and dispense devices for family planning.
- Dispense drugs for treatment of diarrhea, including antihelmintic drugs.
- Application of basic first aid to trauma cases.
- Referral of illnesses to appropriate government health facilities.
- Provide instruction on proper nutrition and dispense food supplements.

Finally, it may be possible to select from among volunteer collaborators suitable candidates for training and work in their own communities as salaried, comprehensive health workers. Such workers and their posts could have the potential of forming the nucleum of a rural health infrastructure.

Promotion of personal protective measures against malaria is perhaps the most difficult type of self-help project to implement. Such measures include screening, repellent, bed nets, adulticiding with "Flit-Guns", and prophylactic use of antimalarials.

The rural population's acceptance of these measures are vitiated by at least two factors. First, the commodities required for personal protection against mosquitoes may be beyond the means of most people in developing countries. Second, even if the required items were to be furnished, their regular use is dependent on a level of sophistication and motivation presently not found in such populations. It might be added that the second factor applies also to population segments of developed countries who live or visit malarious areas since, in recent years, the number of malaria infections acquired by such people have been increasing.

The potential for effective community and personal participation in antimalarial efforts is largely unknown. Of the measures discussed, establishment of volunteer collaborator posts for dispensing antimalarials has the highest probability of success. Implementation of this one measure alone would contribute significantly to the reduction of malaria mortality and morbidity by making antimalarials readily accessible to people in the rural tropics.

In countries with a history of malaria eradication programs where health authorities have made a commitment to continue control efforts, the immediate problem is to convert to a control program. Since budgets, in most instances, will be curtailed at the same time that costs for insecticides, drugs, and equipment will be rising, the revised control strategy must include, at least, the following:

- Upgrade the training of personnel at all levels to emphasize local epidemiologic assessment of the malaria problem.
- Revise and refine the limits of malarious and non-malarious areas since "total coverage" will no longer be possible.
- Develop a national plan which should include objectives, assignment of priority areas, and selection of cost-effective control methods which will not exceed available resources.
- Train personnel (with outside consultants as required) to assess the efficacy of various control methods in representative ecological and geographical situations.
- Develop plans to utilize community and individual participation in malaria control activities.
- Develop a plan with a time table for the integration of the malaria program into the basic health service.

The national malaria team should be headed by an experienced malariologist (Medical Officer). If such a person is unavailable, a candidate with a background in biomedical sciences should be identified and supported during a year-long course in Tropical Public Health. Following this broad training, the candidate must gain experience or, at the least, learn the basics of malariology. Centers where such training was formerly offered, such as the International Malaria Eradication Training Center (METC) in Manila no longer exist.

The current lack of a suitable international training facility for workers in malaria control programs is a serious deficiency. While staff training may not always guarantee program success, without training, no program can get started. A less efficient way of training a medical officer is to have him spend a minimum of three months in a well functioning malaria control program in his region.

Assignment of a foreign malariologist to advise the central team for at least the first 5-6 formative years may be highly useful in most national programs and absolutely vital in others.

A medical entomologist is the second most important member of a central team. As in the case of malariologists, practical training opportunities for this speciality are also difficult to find. A temporary solution being tried by one malaria program is the short-term appointment of an experienced, retired medical entomologist to provide in-country training to local entomologists and assistants.

The third team member required is a sanitary engineer or a sanitarian. Malaria control before World War II (pre-DDT era) relied heavily on engineering methods to reduce mosquito breeding sites. With the advent of DDT, breeding site reduction methods were abandoned. Much can be learned from past experience with these methods for useful application today.

The fourth person needed is a capable administrator, experienced in budget formulation, who can streamline bureaucratic processes to facilitate timely commodity procurement and disbursement of staff salaries and allowances.

Additional subordinate personnel at the central level should include a Parasitologist or a biology graduate experienced in microscopy to be chief of laboratory services; a Statistician to assist the malariologist in the compilation and analysis of data; a Logistics Specialist to assist the administrator in procurement, distribution of supplies and in maintenance of equipment; and a Health Educator to formulate and implement health education policies.

At the field level, a Vector Control Specialist should head a unit which operates from a health center and serves a population of 25,000 to 50,000. The size of the population served depends on population density and ease of road access. The vector control specialist should be a high school graduate at least and have received in-service training in vector control methods. His instructions for malaria control activities should come from the chief of the next higher operational level which serves a population of approximately 500,000. Monthly reports of routine activities should be made to his immediate supervisor: unusual disease occurrences should be reported as soon as possible. In areas where malaria may be a particularly persistent problem, serious consideration should be given to assignment of Peace Corps Volunteers to assist the vector control specialist. The average volunteer's enthusiasm, inventiveness, and his genuine concern for his new neighbors more than make up for his lack of technical experience.

Under direction of the field unit chief and depending on the type of activities undertaken, additional staff members may include an Assistant Vector Control Specialist, whose primary function is to establish, train, and supervise volunteer collatorators and work with community leaders in self-help projects.

Laboratory personnel include microscopists. Those trained during the eradication era should be taught additional, simple laboratory skills, such as white blood cell count and hematocrit determinations, gram and acid-fast staining; Laboratory Assistants trained to staff health centers should be trained to stain and examine malaria smears. If control activities include house spraying, the vector control specialist and his assistant should hire and train available local laborers to implement a spraying program.

In regard to external assistance for malaria control programs, the remarks of a Malaysian colleague made after the 1976 regional meeting on malaria in Southeast Asia held in Bangkok deserves repeating. When asked why the Malaysian malaria program was acknowledged the best in the region, he said: "We were well taught by the British and were fortunate enough not to have received foreign aid." His response underscored the importance of a well-trained staff. Lack of foreign aid was considered a benefit since without external pressures, Malaysia developed her own program at her own pace, and at all times, within her own resources. As a result, progress (while not initially spectacular) was steady and the program was implemented with a notable absence of major administrative or operational problems. It should be emphasized parenthetically that an additional factor responsible for success, perhaps the primary one, is the firm and sustained commitment of the Malaysian government to control malaria.

The primary need is to organize a malaria team at the central level headed by a malariologist (Medical Officer) and assisted by an entomologist, a sanitary engineer, and an administrator with experience in other governmental development programs. Essential data for these personnel to utilize during the planning phase must be gathered and evaluated.

Collect all available epidemiologic data and decide what additional data are needed and what requires updating. Using the epidemiologic data collected, define malarious and non-malarious areas. Develop a plan to control malaria based on available resources and consideration of priority areas for which initial control measures will be emphasized. Based on required personnel identified in the plan of operations, first develop specific curricula with external assistance as required and organize training courses for staff at the various operational levels.

Financial resources comprise an essential factor in planning a control program. In general, the items in a malaria control program that consume more than 90% of the budget are staff salaries and insecticides.

Inflation must be considered. In the past 5-6 years, the price of DDT has doubled and the present cost is 45 cents/pound (75% wettable powder) plus shipping and insurance charges. By comparison, insecticides such as malathion, which must be sprayed more frequently than DDT due to their shorter residual life, have a cost about 3-4 times that of DDT. Other insecticides, for example fenitrothion, are even more costly. The cost of malathion in the malaria programs of Iran and Iraq was estimated to be, 5-6 years ago, between 45-50 cents per capita per annum. Present estimates put the cost at $1 per capita annually. The cost of a chloroquine tablet (150 mg base) in 1977 was approximately 1 cent. Presently, due to a large backlog of orders, the main supplier in the United States will not even quote a price, since the firm will be unable to accept new orders for some time.

Integration of Malaria Control and Other Control Programs

Few disagree on the necessity of combining antimalaria activity with other public health units, particularly vector borne disease control programs. The critical issue is the rate at which the integration process should be pursued. Integration should be

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adjusted to the endemicity of malaria in a given area. If it takes place too rapidly in areas where malaria is highly endemic, the end result is usually a dilution of antimalaria activities and little or no impact on malaria transmission. When integration is undertaken too slowly or not at all as occurred in the late 1960's when eradication activities were discontinued, there are no operational units to keep malaria transmission from increasing once again. The present resurgence of malaria in many instances is due to a failure in effectively integrating antimalaria activities with basic health services. Integration would have made it possible to continue program operations and so maintain the gains which were achieved at considerable cost.

A suggested scheme for merging disease control programs into a Communicable Disease Control (CDC) unit is presented in Figure 3.[21]

The integration of malaria control activities must be carefully timed since uncontrolled malaria in highly endemic areas would swamp existing health centers with so many cases that ability to treat other conditions would be greatly limited. Therefore, integration of the malaria service should be contemplated only when malaria incidence has declined to a level which can be handled by an integrated CDC unit. Just how low incidence should be before integration is implemented is not presently known. The success of integration will depend not only on a reduced malaria case load but on other interacting variables, staff competence and motivation are two examples. In general, it is felt that the criterion used during the eradication era--1 case or less per 10,000 population annually, for integrating antimalaria activities with basic health services is too restrictive for a control program. Some control programs currently use a standard of 1 to 10 cases per 1,000 before adopting integration. The decision depends on the malariogenic potential and the socioeconomic importance of the area, population density, and other factors. The rates mentioned will be approximated only grossly since in a control program, the precision of case detection assumes less importance than during an eradication program.

Major problem areas are itemized here with no attempt to rank them. Any one, if present in sufficient degree, can totally destroy a program.

Undoubtedly, adequacy and stability of financial support will be the major constraint in a malaria control program. The importance of convincing policy makers that malaria control deserves the highest priority cannot be overemphasized. Support funds should come from national resources whenever possible. The continuation of expensive "crash programs" of disease control which rely heavily on external support makes such programs dependent on the vagaries and whims of external politics. Withdrawal of support is often followed by program breakdown and this leaves as a legacy a population particularly susceptible to a disease from which they had been formerly protected.

Availability of trained manpower is another critical area. In most of the African countries, a lack of trained personnel in all disciplines of disease control will be a major hinderance to initiation of malaria control programs. In other countries with a history of malaria control/eradication, the problem is the acute shortage of well-trained and experienced malariologists.

Lack of international training facilities poses a problem. Twenty years ago, no less than five international training centers trained over 2,000 senior staff members for malaria programs throughout the world. Today, not one of these training centers is operational. Ironically, the need to train health workers in the basics of malariology is greater today than it was when the five centers were functional. To meet the urgent need of replenishing the diminished global pool of experienced malaria workers, the international agencies must find the means to reactivate some of these closed centers.

Lack of a single, simple, and inexpensive method of malaria control persists. Unlike an earlier time when spraying house interiors with a residual insecticide was highly effective in reducing malaria transmission, present malaria control strategy utilizes any of a variety of control methods chosen not because of effectiveness but affordability. Unfortunately, no panacea is on the horizon. Those who believe there is--particularly the highly touted malaria vaccine--may repeat the same error which contributed to the failure of malaria eradication, i.e., underestimating the complexity of the problem.

Constant evolution of the malaria parasite and the vector complicates the task. Parasites and vectors are constantly evolving to meet changing conditions. Thus, mosquitoes in some of the malaria problem areas have developed resistance to all available residual insecticides. Likewise the parasite, particularly P. falciparum, has developed resistance to antimalarials, notably to chloroquine. It is obvious that these two organisms, always keeping one step ahead of man, will continue to evolve. For this reason, research in malaria must remain a vital and sustained part of any control program.

The attitude of health workers and the people they serve changes. In more than ten years of overseas service in Africa, the Far East, and Central America, the author noticed that a phenomenon commonly found in developing countries is a communications gap between health workers and the people they serve. There is a pervasive lack of concern for the welfare of villagers. On the other hand, the average villager expects little from government employees and prefers most of the time to be left alone.

Evaluating a Control Program

Malaria control represents a major governmental commitment of financial and human resources usually at the expense of competing programs. Therefore, continuing support for such a program can be justified only if benefits can be documented periodically. Standard malariometric methods used in surveillance have already been outlined. Other useful population measures associated with lowered malaria transmission--especially in malarious countries without prior malaria programs--include a reduction in mortality rate; an increase in the average weight of newborns; a decrease in absenteeism from school; lowered outpatient and hospital attendance; and increases in agricultural and/or industrial productivity.

While the progress of malaria control may be assessed by the methods discussed, it may be difficult to directly attribute program achievements to any single method when a variety of methods are used. This was not the case when house spraying with DDT was the only method used. In areas where the vector was fully responsive to DDT, it was possible to demonstrate that the decline in malaria transmission was directly related to the intensity of spraying. Another problem in quantifying malaria control program achievements is that the major benefits, alleviation of debilitating morbidity and reduction in mortality, lack assigned monetary values.

Many factors, natural and manmade, have a significant impact on the outcome of a malaria control program. A few major ones are adverse climate, development activities, and migrations of people and vectors.

Heavy rainfall may provide abundant breeding sites for vectors. The most dramatic malaria epidemic in modern times occurred in Ethiopia in 1958. An estimated 3.5 million cases, mostly falciparum malaria, occurred in a population of between 8-10 million.[22] The major factor responsible for the epidemic was an annual rainfall which exceeded precipitation noted in records for any previous year. Associated with this epidemic was an unusually high mortality rate which reached 20% in some areas. Drought conditions during 1957 gave rise to widespread famine and an already weakened population when the epidemic struck.

Passage of a hurricane over Haiti in 1963 was followed in 6-8 weeks by a malaria epidemic which resulted in at least 75,000 cases and which obliterated the gains made in two years of DDT spraying in the affected area.[23]

Reduced rainfall may also cause problems. In the famous Sri Lanka epidemic of 1967-68, an estimated 2 million cases occurred. A major causative factor, paradoxically, was an abnormally dry rainy season which gave rise to pools in countless depressions in river beds and a tremendous increase in breeding areas (ordinarily not present in a fast-moving river) for the vector, A. culicifacies.[24]

Economic improvement schemes in developing countries often involve modification of water resources. Irrigation projects and dam construction are two outstanding examples. When planning for these projects, the possibility that an increase in water supply may result in changes in the number and species of disease transmitting vectors must be kept in mind. Plans should include provisions to monitor and respond to any emerging disease problems.

Two examples, taken from the author's experience, illustrate the importance of changes in water resources and malaria transmission.

A malaria outbreak occurred in a military training camp in Vietnam in 1968. Epidemiologic investigation revealed no malaria cases in an adjacent camp 5 km away while malaria, predominantly falciparum, severely disrupted activities in the affected camp. Attack rates in the two battalions most affected were 204 and 217 per 1,000, respectively. It was further determined that these two battalions were those closest to several sizable fish ponds which had been created only recently for the demonstration of fish culture methods. Anopheles sundaicus larvae, the presumed vector, was abundantly present in these ponds.

In a recent trip to El Salvador, the author visited a lake newly formed after completion of a hydroelectric dam. Anopheles albimanus breeding in the lake was responsible for a malaria outbreak in a community adjacent to the lake. Prior to the recent episode, malaria transmission had not occurred in this community for many years.

Migrating people may pose control problems by bringing malaria with them. Particularly important is the spread of chloroquine resistant falciparum malaria into areas where such strains have not previously existed.

Migration of the vector must also be considered. It should be recalled that in 1930, before the present era of rapid transportation, A. gambiae found its way from West Africa to Brazil where it caused severe malaria epidemics. Ten years of intensive effort were required to control outbreaks and eliminate the mosquito.[25]

Methods of evaluation include internal and external reviews. A method of internal evaluation should be developed and used to assess progress of malaria control on a yearly basis at a minimum. Where available, standard surveillance data may be used. When such data are unavailable, other indicators, such as infant mortality or health center attendance records, may prove useful.

External sero-epidemiologic assessment must be considered. Until more practical serologic methods are available for routine use by personnel in developing countries, present methods can be performed only by experienced personnel in established laboratories. Serologic tests, such as the IFA and the IHA performed periodically in an indicator population not more than once every two years, will provide information which will be more objective and more reliable than any other single survey method. Such serologic methods have the following advantages:

- Evidence of infection is not dependent on the presence of patent infection. In a sense, antibodies to malaria mirror the infections acquired over a period of time.
- Increases in antibody titer with time indicate active transmission. The proportion of individuals in the indicator population who show elevations of antibody titer can be related to the degree of malaria transmission.
- The relative proportions of the different species of malaria may be determined.
- In contrast to blood smear surveys, far fewer serum samples are required to obtain significant results.

External program reviews are helpful. Periodic reviews of malaria programs by staff members of WHO and AID have historically been part of every malaria program supported by these two organizations. The concept of utilizing foreign experts to evaluate programs and advise local staff is still sound. The utility of such reviews may be improved by the following:

a. Less frequent reviews. When reviews are held once a year, much of the program staff's time is diverted from their primary duties to prepare and assist in the review.
b. Fewer and more carefully chosen team members.
c. Function of team members should be expanded and time alloted to provide in-depth consultation and/or conduct field research, such as supervising collection of bloods for sero-epidemiogic surveys.

Data on the cost-effectiveness of malaria control programs is presently unavailable: the concept that control measures should be selected on the basis of local epidemiologic conditions and local resources has yet to be implemented. The control method still most widely used is house spraying with residual insecticides. Analysis of cost-effectiveness must become an important and permanent part of future evaluations of malaria programs.

Many major achievements of malaria programs, as has been indicated earlier, cannot be quantified. Those achievements due to a control program which can be quantified are the cost of treatment or hospitalization avoided because of reduction in malaria infections and the cost of work days lost due to illness from malaria.

Gross estimates of time lost to malaria are available. In Africa, it is estimated that malaria causes an average reduction of 20-40 working day/person/year. Recent studies in El Salvador estimate that the patient is bedridden for an average of three days for each attack of malaria. While these estimates may be used to calculate wages lost due to illness caused by malaria, such data has little significance in developing countries where generally the labor force is overlarge and underutilized.

The major justification for supporting malaria control programs must be humanitarian concerns. It should be stressed that most of the one million estimated deaths per year due to malaria are preventable by a treatment which for the average child costs between 1-2 cents.

By virtue of its complexity, magnitude, and seriousness, malaria control poses the greatest challenge in public health today. All people living in developing countries are entitled to that most basic of human rights--to survive beyond childhood, to lead healthy and productive lives.

To summarize, a malaria control program requires a commitment of indefinite duration. For many of the malarious countries, the final stage--eradication of the disease--may come as it did in many of the developed countries, only when socioeconomic development has reached a point where the population enjoys a standard of living far above the mere subsistence level. Until that day, constant vigilence to reduce mortality and excessive morbidity due to malaria must be the primary aim of a control program. To accomplish these basic aims within the economic resources of each country will require training and health education of people, including malaria and public health workers, medical students, policy makers, and, above all, the malaria victims themselves. In addition to training, research is essential to find cost-effective methods to attack the malaria problem. It is certain that many of these countries will need external technical and perhaps financial assistance in the training of a cadre of public health workers, in the organization, and in the initial stages of program operations.

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ONCHOCERCIASIS

by

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Onchocerciasis or "river blindness" is an arthropod-borne, parasitic disease caused by the filarial nematode worm, Onchocerca volvulus. The infection is transmitted from man to man by the bites of black flies (Diptera: Simuliidae). The disease is related biologically to the two other common filarial infections of man caused by Wuchereria bancrofti and Brugia malayi. This paper describes the parasite, the vector, and the disease. It also discusses essential features of the epidemiology and other factors relevant to surveillance and control procedures.

The adult parasite worms, males and females, are long (20-30 cm), threadlike and live in nests or nodules in subcutaneous connective tissue, rarely in deep connective tissue, e.g., joint capsules. The female, which can live for 15 years, produces millions of embryos called microfilariae, that are unsheathed, measure 250-300 u in length and are 6-8 u wide. Microfilariae may be found in all body tissues but are concentrated in the skin where they may live for as long as two years.

Adult worms and microfilariae, depending on the geographic strain of the parasite, show a pronounced tendency for concentration in distinct body areas. In Africa, worms are concentrated in the skin of the lower trunk and legs while the Guatemalan strain is more heavily concentrated in the upper part of the body, the arms, neck, and head. This is probably related to the feeding preference of the respective vectors for these body regions.

Microfilariae are ingested by black flies while taking a blood meal. Black flies, unlike mosquitoes which penetrate and imbibe blood from surface capillaries, anchor their mouthparts into the skin and lacerate it. Blood, tissue fluids, and microfilariae well up into the laceration and are ingested. The microfilariae penetrate the gut of the fly, eventually reaching the thoracic flight muscles. Here they pass through two larval stages (first and second) and develop to third stage infective larvae in 6-8 days after ingestion. The speed of larval development depend on the ambient temperature. Infective larvae migrate to the head capsule and are transmitted to the human host when the black fly feeds again. There is no reproduction of the parasite in the vector so that one microfilariae cannot develop into more than

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one infective larvae, a factor important to the epidemiology of the disease.

Onchocerciasis is a cumulative parasitic infection; serious disease is produced only after prolonged exposure to the bites of infective flies. Many lightly infected persons have microfilariae in the skin but do not have clinical manifestations.

Most of the signs and symptoms of onchocerciasis are attributable to the presence of microfilariae in tissues. These include a variety of dermal lesions, some lymphatic and systemic effects, impaired vision, and blindness.

Early onchocercal dermatitis is accompanied by altered pigmentation (usually hyperpigmentation), itching, scratching, pruritus, and edema. In long standing, intense infections, depigmentation, particularly over the shins is common, along with lichinification and atrophy. The latter, together with edema produces the leonine facial features seen in Mexico and Central America.

Lymphatic and systemic involvement results from the spread of microfilariae to body tissues other than connective tissue. Lymphadenitis of the inguinal lymph nodes may produce hanging groin and elephantiasis of the genitalia. Microfilariae are also found in the sputum, blood, urine, and spinal fluid of heavily infected persons.

The most serious consequences of onchocerciasis are ocular lesions caused by microfilarial invasion of the eye, which results in impaired vision or blindness. The prevalence and severity of eye lesions are directly related to the intensity of infection. The types of eye lesions produced are: (1) "fluffy" or "snowflake" corneal opacities resulting from a cellular reaction around dead microfilariae in the cornea; (2) sclerosing keratitis; (3) anterior uveitis; (4) choroidoretinitis; (5) optic neuritis and post neuritic optic atrophy. Lesions in the anterior segment are about three times more frequent than in the posterior segment. Sclerosing keratitis is the lesion most frequently responsible for blindness. The lesion is caused by the death of many microfilariae in the cornea over long periods of time.

The same types of lesions occur in Central and South America as in Africa but are more prevalent and intense in the latter area. In West Africa, the strain of parasite found in the dry savanna region produces more blindness than the coastal rain forest strain. The difference is due mostly to the greater prevalence of sclerosing keratitis in the savanna.

Onchocerciasis can be diagnosed by palpation for nodules that contain adult worms, demonstration of microfilariae in skin biopsies, detection of microfilariae in urine, or by the Mazzotti test.

In Africa, examination for nodules alone is not a sensitive method as many people have microfilariae in the skin but no detectable nodules. This is probably due to the location of adult worms in deep rather than subcutaneous tissue. In Mexico and Guatemala, the early appearance of the nodule, particularly on the head is a common feature in infected individuals and many younger persons will have nodules before skin microfilariae can be detected. Most prevalence data from these areas are based on nodule rates and provide valuable information on the geographic distribution of infection.

The skin biopsy is the standard method for parasitological diagnosis and is both a qualitative and a quantitative technique. The usual procedure is to take one or more superficial biopsies with a sclerocorneal punch (the Holth type is recommended) from the areas of the body where microfilariae are concentrated. The optimum site for the biopsy depends on the geographic strain of the parasite as noted earlier. These are the iliac crest in Africa and South America, the ankle in the Yemen, and the shoulder in Mexico and Guatemala. Biopsies are incubated in water or preferably saline and the emerged microfilariae counted after a certain interval of time. The usual incubation time is 30 minutes; however, recent studies have shown that four hours or more gives more sensitive and comparable results.

Biopsy incubation is carried out on microscope slides or in microtiter wells. When the size of the biopsy is uniform or if the individual microfilarial count is adjusted for biopsy size (by weight or area), a quantitative measure of intensity of infection is obtained. This is most often expressed as the geometric mean number of microfilariae per milligram of skin (mf/mg) and correlates well with the prevalence and severity of clinical manifestations including eye lesions.

Two other species of filariae inhabit the human dermis. In certain areas, microfilariae of O. volvulus must be distinghished from those of Mansonella ozzardi and Dipetalonema streptocerca. If blood is taken with the skin biopsy, microfilariae of D. perstans and Loa loa may be encountered also. Microfilariae can be fixed in 2% formalin, spread on a microscope slide, dried, and stained for differential diagnosis.

The mazzotti test is used routinely for diagnosis in Mexico and Venezuela. It consists of administering a single oral dose of diethylcarbamazine (usually 50 mg) and observing for skin rash and itching 3 to 24 hours later. Diethylcarbamazine is a potent microfilaricidal drug that provokes an allergic reaction to the dying cryptic microfilariae. The Mazzotti test is useful for identifying infected persons in whom the parasite cannot be demonstrated directly by skin biopsy or by palpation for nodules. It should not be administered routinely as severe reactions can occur in persons with intense infections.

The vectors of Onchocerca volvulus are biting Diptera of the family Simuliidae (black flies or simuliids). In Africa, the parasite is transmitted mainly by members of the Simulium damnosum (subgenus Edwardsellum) complex. In eastern and central Africa, however, species of the S. neavei (subgenus Lewisellum) complex are also vectors along with S. damnosum. In the western hemisphere, several distinct species of Simulium have been implicated. In Guatemala and Mexico, S. ochradeum is the primary vector but S. metallicum and S. callidum are considered secondary vectors. In the northern and eastern foci of Venezuela, S. metallicum is the primary vector and S. exiguum may be secondarily involved in transmission. In the newly discovered foci on the upper reaches of the Orinoco River in Venezuela and Brazil, S. pintoi and S. amazonicum have been implicated. In Colombia, S. exiguum is presumed to be the vector.

Species complexes exist. Simulium damnosum and probably also S. neavei are not single entities but are made up of several closely related species or subspecies. Until recently, these could be identified only by examination of the polytene chromosomes found in the salivary glands of the larvae. Eight such "cytotypes" have been described as species and six can now be identified by antennal and wing characters. The importance of this lies in the fact that only certain cytotypes are involved in human onchocerciasis transmission; the remainder are mainly zoophilic. Furthermore, each cytotype has its characteristic behavior and ecological requirements.

The aquatic stages of black flies inhabit a wide variety of streams in different bioclimatic zones that reflect the ecological requirements of each species. These range from tiny rivulets no more than a few inches wide for S. ochraceum to very large rivers for some members of the S. damnosum complex. In general, breeding occurs in swift running, well oxygenated, unpolluted water. The larvae attach to various submerged supports (vegetation, rocks, debris, etc.) by means of a posterior sucker armed with hooks. The duration of the aquatic stages depends on water temperature and requires 10-12 days for the West African species and up to 30 days for S. ochraceum at the higher elevations in Guatemala.

Larval Simuliidae have plumose fans on their mouth parts that filter out particulate food from the flowing water. Ingestion is indiscriminate and larvae will take in insecticide particles as well as other matter.

Female black flies bite from dawn to dusk, usually outside of houses. Except for S. ochraceum, which feeds mostly above the waist, vector black flies prefer to feed on the lower parts of the body. Biting is not constant throughout the day and unimodal or bimodal biting curves have been described for several species.

The abundance of flies may show marked seasonal variations related to the productivity of the breeding sites. Fly production usually fluctuates according to the water level and flow rate. For example, the high water levels during wet season in Guatemala make the streams unsuitable for attachment of larvae and peak populations occur at the end of the rainy season when streams subside. In Africa, adult fly populations may vary inversely or directly with water level and flow rate depending on the species and the stream type.

Adult females can disperse considerable distances from the breeding sites by flight, on a prevailing wind, or by both methods. In the Onchocerciasis Control Program of the Upper Volta River Basin, West Africa, flies have travelled distances of 150 km or more to reinvade areas where breeding was apparently controlled. The Central American vectors have maximum flight ranges of 10-15 km.

The longevity of adult females is not known precisely but probably does not exceed a month for both S. damnosum and S. ochraceum. A higher proportion of older females are found within 1-10 km of the breeding sites: this makes transmission more intense at the stream banks where people congregate to fish, bathe, wash clothes, and obtain drinking water.

Geographic distribution is widespread. Endemic foci are found in tropical Africa, Yemen, Mexico, Guatemala, Venezuela, Brazil, and Colombia. The vast majority of cases and the largest affected areas are to be found in Tropical Africa within the latitudes 15°N and 15°S. The worldwide and regional distribution of onchocerciasis has recently been reviewed by a WHO Expert Committee (1976) and by Sassa (1976).

The total number of infected people worldwide probably approaches 40 million, with the vast majority of these in Tropical Africa. An example of regional severity is provided by the Upper Volta River Basin of West Africa. This area covers about 700,000 km^2 with an estimated 10 million inhabitants; 70,000 are blind and many more have severe visual impairment due to onchocerciasis. In addition to ill health and misery, the disease can produce severe, adverse economic effects on the population. In certain areas of Africa, the breeding sites of the vectors, where transmission is most intense, are the fertile riverine valleys of the arid Savanna. The intense transmission causes the inhabitants of these areas to abandon their villages and fields and migrate to less fertile areas that cannot provide an adequate subsistence. Thus, the most productive lands are rendered unusable and uninhabitable by the disease.

The public health importance of onchocerciasis in Latin America has been recently reviewed by PAHO (1974). In general, it is less important than in Africa except in certain foci where transmission is intense or where economic and agricultural development is in progress. In Guatemala, for example, the endemic areas cover 5,000 km^2 and 10% of the estimated population of 300,000 are infected. In the more heavily infected vaillages (or coffee plantations), 90% of persons are infected, 15% have onchocercal eye lesions, and 3-4% are bilaterally blind. In Mexico, Guatemala, and the northern and eastern foci of Venezuela, the disease is associated with the cultivation of coffee on the slopes of volcanic mountains. There are no data on the economic and socio-cultural effect of onchocerciasis on coffee production or coffee workers.

Epidemiological Patterns

The patterns of infection and disease in a population are directly related to the cumulative amount of exposure. Furthermore, these patterns are similar in hyperendemic areas regardless of the geographic area. Infections, depending on the intensity of transmission, are usually first detected in young children 1-4 years of age. The prevalence increases rapidly thereafter and approaches 100% during the beginning of the second decade of life. The intensity of infection, as measured by the microfilarial skin density, continues to rise after maximum prevalence is reached.

Sex differences in the prevalence and intensity of O. volvulus infection are most pronounced in hyperendemic areas. In general, maximum prevalence in females is attained at an older age, the maximum microfilarial skin density if lower in females than in males, and eye lesions and blindness are more common and severe in males than in females. It is unknown whether these differences are due to greater exposure of males or greater susceptibility of males to the parasite.

There is a close association between levels of endemicity, intensity of infection, and visual impairment due to onchocerciasis. In hypoendemic areas, serious onchocercal eye disease is uncommon and due mostly to posterior segment lesions. Uveitis and posterior segment lesions are more common in mesoendemic areas and some blindness may occur. In hyperendemic areas, sclerosing keratitis is the most common eye lesion and blindness rates often reach 5% of the total population.

While the types of eye lesions are the same regardless of geographic strain, the prevalence and severity of sclerosing keratitis and blindness are greater in the savanna regions of West Africa than in the West African rain forest or in Latin America. In Africa, these differences are due to the greater pathogenicity of the savanna strain and not to differences in intensity of transmission.

Onchocerciasis is a highly focal disease that occurs around black fly breeding sites where the distribution of foci depends on the hydrogeographic characteristics of the region. Where breeding sites are contiguous and frequent, the focus may be large and continuous as in the African rain forest or in Guatemala. Where breeding sites occur along river courses in semiarid regions as in West African savanna, foci tend to be discrete and closely follow the river valleys.

Large differences in endemicity can be found between populations located only a few miles apart and are directly related to the proximity of settlements to breeding sites. Not only are there more flies that attack settlements closest to the water, but the flies are older and more likely to be harboring infective larvae. This has led to the classification in Africa of first, second, and third line villages according to their proximity to breeding sites. These villages show striking differences in the age patterns of prevalence and in the frequency of eye lesions and blindness in adults.

Estimate of the Current Problem

Existing data on onchocerciasis come from two sources: the organized control programs in Africa and Latin America and from time-limited prevalence surveys that are of an investigational nature. Survey data are usually published in scientific journals, and a careful search of the literature can provide valuable information on the prevalence and severity of infection and on vectors in limited geographic areas. Often, however, independent research teams have used different methodologies so data are not comparable with earlier work or with different geographic regions. Further, they seldom provide complete information on the magnitude of the problem. One is usually left with the question of how extensive the affected area is or how many people in the area are at risk of infection. If the survey techniques are sound, the data remain timely for a good while because of the chronic, slow evolution of the disease.

Data from Latin America come from the treatment programs that have been in effect for several decades. In Guatemala, diagnosis and treatment consists of a search for and removal of palpable nodules. In Mexico and Venezuela, the Mazzotti test, skin biopsies, and chemotherapy are also applied. The geographic extent and intensity of infection are gauged by the prevalence of nodules in the population and how quickly new nodules reappear in treated persons. This information, together with investigational data provides a reasonably accurate estimate of the current problem.

In Africa, the ongoing Onchocerciasis Control Program in the Upper Volta River Basin provides the best example of completeness of data on the disease and its effect on the population and economy. No attempt will be made to review this extensive work here; the reader is referred to Report of the Preparatory Assistance Mission to the Governments (PAG) and its annexes (1973) available through WHO, Geneva.

In other areas where the distribution and severity of the disease is poorly defined, prevalence surveys are required to define the existing situation. Surveys should include the use of quantitative skin biopsy diagnosis, examination of the body for nodules, a simple examination for visual impairment, and the collection of anthropophilic black flies. Where visual impairment is discovered, the specific etiology should be determined by ophthalmologists.

In countries where control is contemplated, an inventory of the resources available for combating the disease should be made. Since control of vectors is the only practical means of disease control, particular attention should be given to other existing vector-borne disease control programs (malaria, filariasis). Such an inventory is useful for defining the commitments that a country can make to a control program and in deciding on the necessity for requesting financial and/or technical assistance from outside agencies (WHO, AID, etc.).

In Africa, with the exception of the OCP, there are few programs that adequately meet the problem of onchocarciasis and few countries that have adequate resources to launch an effective program by themselves. The programs in Latin America have already been mentioned and rely on treatment of individuals rather than vector control. In some cases, these programs have not been adequately evaluated so that their effectiveness in the prevention of disease is uncertain.

The only practical means for mass control of onchocerciasis in Africa is by the application of larvicides to the breeding sites of the simuliid vectors. Past programs, particularly against S. neavei in Kenya, have shown that this line of attack can successfully stop transmission if systematically applied for a sufficient length of time.

Chemotherapy with suramin and diethylcarbamazine is useful for the treatment of individual cases under close medical supervision. Suramin kills both adult worms and microfilariae but is highly toxic and fatalities due to exfoliative dermatitis and renal failure have been reported on several occasions. Diethylcarbamazine is a potent microfilaricidal drug of low innate toxicity that is quite useful for mass administration in campaigns against the blood-borne filariae (W. bancrofti, Brugia spp.). With ochocerciasis, however, it must be administered under close medical supervision with steroid cover because of the severe allergic reactions that occur in response to the death of microfilariae in the skin. This immunologically mediated pathology is poorly understood, but involves release of microfilariae antigen upon the death of the microfilariae which causes mast cell degranulation, histamine release, local and systemic anaphylaxis, and the formation of antigen-antibody complexes.

Denodulization campaigns in Latin America have been the basis of control for several decades. The statement has been made that the prevalence and severity of eye disease have been reduced but that nodulectomy has not affected the prevalence of infection. However, recent studies have shown that the prevalence of eye lesions and blindness are still unacceptably high in hyperendemic areas of Guatemala where nodulectomy has been carried out systematically for several years. While nodulectomy cannot be recommended as a single control method, it may have some role in Guatemala and Mexico in prevention of eye disease and reduction of transmission in conjunction with vector control.

The objective of a control program should depend on special characteristics of the endemic foci concerned. At a minimum, the objective should be the reduction of transmission to a point where onchocerciasis is a minor parasitosis causing no eye disease. This is probably the most practical objective for the widespread and intense foci of West Africa where the landscape and flight range of the vectors make it extremely difficult to stop transmission altogether.

Where foci are more circumscribed and accessible and the vectorial capacity of the simuliids is low, complete cessation of transmission may be possible. In Kenya, eradication of S. neavai was achieved in an isolated focus by repeated treatment of the breeding sites with DDT. Vector eradication, however, is usually not an attainable objective.

A control program must be based on adequate information that includes epidemiologic, entomologic, and demographic data. Often these data are not available and must be collected during initial surveys carried out to define the existing situation or in the preparatory phase of the control program.

Epidemiologic data includes parasitological examination of statistically valid samples of the population in different geographic areas. These provide data on geographic distribution of the infection; age and sex specific prevalence rates; intensity of infection by age and sex; prevalence of nodules by age, sex, and location on the body; and eye disease due to onchocerciasis by age and sex.

Entomologic data provides knowledge of which of the simuliids in the area are contributing significantly to transmission. Maps also locate the breeding sites of vectors.

Demographic data includes an accurate census of the population and maps which show villages and their proximity to breeding sites; migratory status of population; and economic importance of areas; i.e., most productive agricultural land.

Control Program Timetables

It is difficult to formulate precise, standard timetables because each program must be devised according to the magnitude of the problem, available funds, and management structure. In any case, it must be thought of as a long term program for interrupting transmission by vector control. Where the focus is small and isolated and complete cessation of transmission can be maintained for 20 years (the life span of the female worm), all infections should be resolved and vector control can cease. Control programs in other areas will have to be continued indefinitely.

If it is assumed that the magnitude of the problem has been defined and long term funding is assured, the following general timetable is suggested.

Preparatory Phase--2 years: Appointment of the program director and three unit directors for vector control and surveillance operations, epidemiologic surveillance, and administrative support services. They will:

- plan budgets and staff requirements.
- acquire physical facilities and equipment for central offices, laboratories, and field survey teams.
- recruit professional and technical staff including a statistician/computer specialist.
- secure larvicide and application equipment. Abate (0,0 -(thiodi-4, 1- phenyl) 0,0,0,0 -tetramethylphosphorothicate) is the best available at the present time. Application equipment may include fixed wing aircraft or helicopters.
- formulate long term training programs. Nationals should be brought into the program early on for training and work experience.
- collect entomological baseline data for at least one full annual cycle. This should include adult biting rates and infectivity rates at sites selected for future surveillance.
- conduct preliminary tests with larvicides to determine the most effective methods and rates of application and the sites for application.
- within the epidemiology and vector control units, plan and budget for research on problems that are likely to arise or aspects that may accelerate control. This research should include studies of insecticide resistance by black flies, adverse ecological effects of pesticides in rivers, development of more effective chemotherapy, and development of non-chemical means of vector control (habitat alteration, biological control, etc.).
- assemble expert advisory panels on insecticide development and insecticide resistance, on the ecological effects of the long-term application of pesticides to river ecosystems, and on non-chemical means of control.

Control Phase--3 years: The length of the control phase will depend on the size of the area under attack. For example, the OCP area of 700,000 km^2 was divided into three sectors that were brought into the control phase one at a time over three years. Initially, larvicide is systematically applied to all breeding sites within the area to reduce and maintain transmission to the desired level as defined by the objectives. The entomological surveillance system (see following section) provides the means for evaluation of the insecticide application. When transmission has been maintained at the level as defined by the objectives for a sufficient length of time (at least one full annual cycle), the maintenance phase can begin.

Maintenance Phase--15 years of more: The intensive, widespread insecticide coverage of all breeding sites within the control area can be replaced with the application of insecticide to only certain problem areas where breeding continues and around the periphery of the control area to contain repopulation from neighboring endemic zones. The maintenance of a complete and timely entomological surveillance system is vital.

Disease surveillance in a control program should be planned within the time frame in which changes can be expected. Because of the chronic, slow evolution of onchocerciasis, it will be at least 3-5 years before infection and disease can be expected to diminish. Selected populations should be monitored every 3 years for changes in prevalence (biopsy positivity) of infection and more intensively, every 5 years for changes in disease patterns (nodule rate, prevalence and intensity of skin infection, eye infection and eye lesions). In the selection of study populations, it should be kept in mind that simple, error-free indices of change are required; they should be relatively easy to obtain yet permit valid comparisons between populations and with precontrol data. Survey populations should include the younger age groups and those groups most at risk to infection. The format for the collection, recording, and analysis of these data has been published by WHO (1974).

Entomological surveillance is the principal means of evaluation throughout the length of the control program. Furthermore, it provides the information necessary for deciding when and where to apply insecticide. Both adult and larval populations are monitored; however, because of the inaccessability of many of the breeding sites and because transmission can be measured directly, the important measurements are those of adult fly populations.

Parameters for surveillance include total biting density, the absolute number of adult female flies that would bite a single man under standard conditions of exposure. It is usually expressed as the number of flies per man per month or per year. Infective biting density refers to the proportion of the total biting density that is harboring infective larvae of O. volvulus. Transmission potential is the total number of infective larvae harbored by the infective flies. It is the product of the infective biting density and the arithmetic mean number of infective larvae per infective fly.

In practice, a person sits at a collection site and collects, before he is bitten, all flies that land on him during the day. These are identified and counted and a sample disected to determine the proportion harboring infective larvae and the mean number of infective larvae per fly. This is done for several days each month at several sites within the control area. Collection sites should be near human settlements where precontrol data have shown biting rates and transmission potentials to be highest. These are usually near the most productive vector breeding sites.

As these parameters are directly related to the cumulative amount of infection and disease in a community, it is possible to estimate the reduction in vector populations required to reduce onchocerciasis to a minor parasitosis. This estimate should be made in the preliminary phase and consists of measuring biting densities and transmission potentials in nonendemic areas and in hypo-, meso-, and hyperendemic areas where the amount of onchocercal disease has been determined.

An outline of resources required for an effective program includes various elements. Central offices are required for administrative services that should also house the data processing and communication units. As aircraft may be used, fueling and maintenance facilities are required.

Field units are required for both the vector control and the epidemiology units. Sturdy vehicles, tents, electrical generators, and other camping equipment are necessary for extended surveys. The epidemiology unit will need portable slit lamps, direct and indirect ophthalmoscopes, sclerocorneal punches (Holth type), microtiter plates, saline, and forceps. A basic dispensary should be carried so that people can be treated for common ailments. In addition to providing some medical care, this guarantees the future cooperation of the sample population.

Laboratory facilities are needed for dissecting flies and for any clinical follow-up or drug treatment that may be done. Dissecting flies is tedious work and the best microscopes available should be purchased for this task. It will be less expensive in the long run and more accurate data will be obtained. Likewise, the laboratory should be a comfortable, pleasant facility.

As onchocerciasis control is a long-term undertaking, nationals should be brought in for training early on in the project. This will help prepare the local health authorities for taking over the program during the maintenance phase. Personnel should be trained in administration, entomological and epidemiological surveillance techniques and in the safe handling of insecticides.

The need for an applied research function to be built into each operational unit has already been stressed. A committee of experts should be convened to identify research needs and priorities relevant to the control program.

Staffing within the program has already been discussed. Outside consultants should be available if unusual problems arise that cannot be dealt with internally. Because the intensive epidemiological studies are carried out at 5-year intervals, it may be possible to use outside staff for these operations.

During the preliminary and the control phase, a large scale onchocerciasis control program should be kept separate from other disease control efforts with a vertically integrated management structure. Once transmission is controlled and the maintenance phase is reached, it may be possible to integrate it into the national health unit that deals with vector-borne diseases. In most countries where onchocerciasis is a major public health problem, a control program can be mounted only with the direct involvement of international agencies to provide a stable source of long-term funding, trained people, and the necessary technology.

Major problems expected are equally varied. For instance, eventual black fly resistance to insecticides must be anticipated since long-term application is required. Fly populations should be monitored continuously for signs of resistance. A systematic search for new insecticides and new control methods (e.g., biological, physical, etc.) should be initiated at the beginning of the control program.

The same rivers that breed black flies also provide water for drinking and domestic use as well as fish for food. It is therefore, important to determine (or at least estimate) the toxicity and ecological effects of insecticide application.

Political and economic instability will adversely affect the outcome of a long-term control program: in Uganda, for example, political upheaval terminated an otherwise successful control effort. While little can be done to avoid this situation, it should be considered in the selection of an area for control.

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Changes in the breeding sites as a result of agricultural or industrial development could reduce or increase vector populations, depending on the nature of the change. Further, the immigration of uninfected people to onchocerciasis zones or the emigration of infected persons into disease-free areas where potential vectors are present could increase transmission and disseminate the infection. Communication between other appropriate governmental or private agencies responsible for such changes and the onchocerciasis control program should be established.

Problems in maintaining the accuracy of work and enthusiasm of the technical staff should be anticipated. This can be met by close supervision by professional staff and periodic retraining.

Reinvasion of the control area by flies breeding outside it will be a continuous problem. In the OCP, for example, up to 35% of the control area is affected each year. These are older flies, a high proportion of which harbor infective larvae, and are apparently coming from breeding sites 150-220 km away. The entomologic surveillance system together with knowledge of adult fly behavior (flight range, migratory patterns as affected by prevailing winds, etc.) can anticipate the problem and prevent repopulation of breeding sites in the control area. This biological phenomenon argues for a widespread fly eradication program; however, this is probably unobtainable under the conditions that exist in most of Africa. In these intense and large foci, one must plan to maintain long-term interruption of disease transmission. This will require the application of vector controls for the foreseeable future, and until such time as efficacious prophylactic chemotherapy or vaccines are available.

Evaluation of Control and Conclusion

In the short term, the entomologic surveillance will measure the progress of the program. Ultimately, program achievement will be measured chiefly by the reduction or the elimination of visual impairment due to onchocerciasis. Such a reduction in disease will occur first in young children and later in the general population.

The methods for evaluation are built into the program within the entomologic and epidemiologic surveillance units. However, periodic assessment should be carried out by an independent team of experienced persons whose jobs do not depend on the continuation or success of the program.

The most important intervening event that could affect the outcome of a control program would be the discovery of chemotherapy (including prophylactic chemotherapy) suitable for mass administration or a vaccine. These could greatly accelerate the control of transmission and protect persons from infection. Basic research on these aspects should be strongly supported at all levels.

From the standpoint of number of cases worldwide, onchocerciasis is not the most important disease of the tropics. However, in areas where it does occur and transmission is intense, it is the single most important cause of widespread visual impairment and blindness. In addition to disease, its insidious effect of depriving a subsistence economy of the most productive land must be included in any cost-benefit calculations for control. Each individual focus has to be considered separately and control strategies devised that fit the local situation. For example, the eradication in Kenya was successful because of certain biological characteristics that produced isolated foci amenable to an eradication strategy. A similar situation may exist in Guatemala and Mexico. In much of Africa, however, control programs must be planned to continue indefinitely.

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SCHISTOSOMIASIS

by

Donald Heyneman

Schistosomiasis or bilharziasis is a disease due to blood flukes (trematodes) which has plagued mankind for thousands of years. Larval forms of the worms enter through the skin of the host while he or she is wading in infected waters in certain areas in the tropics and subtropics. Bilharz in 1851 discovered the adult worm in the mesentaric vein of an Egyptian in Cairo and later showed the relation of the parasite and its ova to the prevailing hematuria and dysentary among the native population. Today, despite sufficient knowledge of the life cycle, snail transmission in infected water, and methods of presention, the disease has not been well controlled in most developing countries.

The infectious agents responsible for human schistosomiasis are members of the genus Schistosoma which are commonly called blood flukes. The human blood flukes consist of three primary species: Schistosoma haematobium, S. mansoni, and S. japonicum. Each produces a characteristic disease with its own syndrome and pathology. In addition to these species responsible for most cases of human schistosomiasis, another fairly common form, S. intercalatum, has been implicated in isolated foci of infection in Central Africa where it appears to induce very little pathology and is a relatively minor form of the disease.

Still other members of the genus Schistosoma have occasionally been implicated in human infection. These are primarily parasites of cattle in South Africa: their infection in humans is accidental and epidemiologically insignificant. These species include S. bovis, S. mattheei, and S. spindale.

The following, taken from Warren (1971), is a concise and accurate summation of the process of pathogenesis in schistosomiasis: "Basic to an understanding of the disease processes in schistosomiasis are these facts: The schistosomes do not multiply in man; complete immunity does not follow initial infection; repeated infections usually occur; the worms are long lived; large worm burdens may gradually accumulate; and a large proportion of schistosome eggs are not excreted but remain within the body. Disease is related not only to the presence of the various stages of the schistosomes in the body tissues and their secretions and

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excretions, but to the inflammatory responses of the host as well.

"Clinically, three distinct syndromes occur at different stages of schistosome infection. Within one day of cercarial penetration, swimmers itch, a pruritic papular self-limited but possibly fatal illness resembling serum sickness, may develop. Finally, after many years during which the infection may be asymptomatic associated with relatively mild intestinal or urinary tract symptoms, fibrosis of the liver may result in the signs and symptoms of portal hypertension in schistosomiasis mansoni and japonica; fibrosis of the ureters and bladder in schistosomiasis haematobia may result in changes associated with urinary tract obstruction."

Fundamentally, schistosomiasis is a disease that results from a host-parasite imbalance in which gradually increasing host sensitivity to the presence of foreign antigen, chiefly schistosome eggs and their products within the tissues, induces a cumulative response that we observe as chronic schistosomiasis.

Schistosomes are able to induce a large number of conditions depending upon the distribution of the fomenting eggs, which can be passed to any part of the body. The disease that results is essentially a response of the host to the antigenic material and is usually focalized in the organs primarily affected: bladder, intestine, and liver. Additional systems or organs may be affected, particularly following collateral circulation distribution. In most cases, these are minor or perhaps unrecognized; but where lung, heart, and brain are involved, the result may be fatal. Cutaneous involvement is a distressing indicator of the astonishing variety of conditions that may be induced by products of these parasitic worms.

A definitive diagnosis requires presence of eggs in feces--or urine in the case of S. haematobium. In a biopsy specimen, usually taken from the rectal region in cases of S. mansoni, the eggs are characteristic and easily identified when visible in tissue sections. Identification of eggs in a simple fecal smear is usually insufficient in light infections. Various concentration techniques, such as the formol-ether method, permit a concentration of roughly 25 times. The Kato method is a useful procedure for employing larger samples of fecal matter than can be examined under one slide smear preparation. It is also adaptable for quantitative methods. Diagnosis of schistosomiasis haematobia requires collection of a urine sample, preferably at midday as diurnal variation in egg output has been demonstrated. The specimen is centrifuged and the sediment examined. Concentration sediments can be diluted with distilled water to test viability by demonstration of eggs hatching and as a means to diagnose low-level infections. Eggs can also be examined by a counting technique, such as the Bell method which involves dilution of the sample, sieving onto filter paper, followed by ninhydrin staining. This method can be applied either to urine or feces.

Counts of ninhydrin-stained eggs trapped on filter paper circles are being more frequently employed for accurate detection of infection level. Physicians may use knowledge of infection level to decide whether or not treatment is indicated.

Severity of intentinal disease can be determined directly by sigmoidoscopy: barium enema may also be useful. Liver disease is determined by liver biopsy, by the barium swallowing test, esophagoscopy, and particularly by splenoportography which measures intersplenic pressure. In the case of S. haematobium, cystoscopy and pyelography are important indicators of infection level.

A rectal biopsy may be of great use in the diagnosis of S. mansoni or S. japonicum infection and may even pick up S. haematobium eggs on occasion. It consists of small snips taken through a proctoscope, pressed between glass slides, and immediately examined microscopically. The test is also a useful indicator of egg viability which, in turn, suggests whether or not the worms are alive. If only opaque, dead eggs or shells are observed, the parent worms are probably absent or dead. If eggs containing a miracidium are seen, there is no doubt that living worms are present and treatment is justified. Other indications of recent exposure useful in diagnosis include dermatitis following suspected exposure in fresh water, fever some weeks after exposure, or sosinophilia, a particularly useful sign of schistosome infection. In suspected S. haematobium cases, hematuria, dysuria, or frequency are important indicators.

Various skin tests have been developed for the diagnosis of schistosomiasis. Most are suitable only for a general indication of past infection or levels of infection in populations since false negatives and false positives may occur. Most of these tests are of the immediate sensitivity type, convenient to use, involve small amounts of antigen, and can be read quickly. However, the major problem of antigen purification impedes development of a truly specific diagnostic test capable of discriminating among cross-reacting antigens. Several enzyme-specific antigen derivatives have been developed which give promise of diagnostic specificity, but these are still experimental.

A number of immunological methods based on detection of circulating antibody are available but are of little value in the diagnosis of individual infections. As with skin tests, cross reactions with other parasitic infections lead both to false positive and false negative responses. However, a large number of serological tests have been devised--complement fixation, flocculation, indirect hemagglutination, fluorescent antibody, and circumoval precipitation tests--and all have been employed for schistosomiasis detection. Other tests, such as the miracidial immobilization serum test, may be useful for experimental or other highly specific purpose. But at the present time, none of the serological methods available are definitive diagnostic tools though several have considerable promise and are under investigation for application in mass or field surveys.

Treatment requires accurate diagnosis and critical evaluation of each patient for:

- presence of living worms,
- estimated number of worms,
- duration of infection,
- probability of reinfection, and
- length of time the individual will be exposed or remain in the endemic zone.

In many instances, infection will be light, no clinical indications will be present, and the decision probably will be not to treat the individual. It is often difficult to decide whether to use the toxic drugs available or to risk the possible development of disease due to chronic infection. Mass treatment in endemic areas is far more difficult because individual follow-up is seldom possible and evaluation of risk to patients over the full age range is essentially impossible. That means the drug selected must be readily tolerated, nontoxic, easy to take, and effective in a single dose: antischistosomiasis drugs have none of these characteristics. Available drugs are toxic, most are injectibles that require multiple doses, they are costly, and have limited effectiveness. Under conditions of poor nutrition, concomitant infection with other parasites, or other stress conditions, these drugs may pose an even greater risk if used for mass therapy.

It may be appropriate to modify our view of "cure" or satisfactory treatment to include a low, presumably harmless level of infection. Recent evidence by Smithers, Terry, and colleagues shows that in experimental animals, a "concomitant immunity" induced by a prior schistosome infection appears to prevent infection on subsequent challenge. Another possibility is to employ drugs primarily for sterilization of worms in order to reduce egg output and subsequent development of disease. It may, therefore, be best not to attempt to eliminate all worms and so avoid the toxicity incurred by the high drug dosages required for their complete elimination. The possible advantages of retaining a small number of sterilized worms to maintain immunity adds to this argument.

The three species of schistosomes that commonly infect humans vary in their response to drugs: S. haematobium is the most responsive to therapy; S. japonicum, the least. Treatment of S. japonicum is limited to the highly toxic antimony compounds, particularly tartar emetic (antimony potassium tartrate).

Antimony treatment dominated schistosomiasis chemotherapy for over 40 years. Treatment was long term and produced many side effects. Niridazola and hycanthone emerged later, the former having the advantage of being the first successful oral treatment and the latter, of giving a high cure rate with a single injection. Both, however, produce side effects which are sometimes severe. Metrifonata emerged as another successful oral treatment with minimal side effects but was successful only in treating S. haematobium infestations and in the unusual presentation of S. mansoni in the urine. Preliminary work in aminals has shown that oxamniquine (Vansil), a tetrahydroquinoline derivative, produces high cure rates in S. mansoni infection with minimal toxicity after a short treatment period. But the dose response in humans varies in different regions. Recent studies in the Sudan by Omer suggests that despite a lower cure rate with a lower oral dose regime of oxamniquine, such a regime which is well tolerated, may be useful in a low cost control program in reducing transmission of S. mansoni infection.

Distribution of the human schistosomes appears to be primarily African in the case of S. mansoni and S. haematobium; whereas, S. japonicum is found in various foci in the Orient.

Today, S. mansoni is found in all countries of Africa except certain portions of North Africa, such as Tunisia, Algeria, Morocco, Mauritania, Portuguese Guinea, Niger, The Congo Republic, Somalia, and Mauritius Island. S. mansoni, along with S. haematobium, has spread to Aden, Saudi Arabia, Yemen, and elsewhere in the Arabian peninsula as well as to countries bordering the eastern Mediterranian. S. mansoni is particularly common in Yemen where about half of the population may carry the disease. S. mansoni has spread as well into the New World where it is the only schistosome found. Apparently it was carried during the slave trade era into Brazil, and from there, it spread to Venezuela and Surinam. It is also found in several Caribbean islands, such as Puerto Rico, Vieques, Dominican Republic, Antigua, Guadeloupe, Martinique, and St. Lucia.

S. haematobium is even more widespread in Africa than is S. mansoni. It is found throughout the continent, including the Malagasy Republic, and is now endemic in Aden, Saudi Arabia, Yemen, Israel, Iraq, Iran, Turkey, Syria, and Lebanon. Its prevalence is probably highest in Iraq where approximately one fifth of the population is thought to be infected. S. haematobium has not succeeded in crossing the Atlantic to South America as has S. mansoni, apparently due to the lack of appropriate intermediate hosts.

S. japonicum is found in China, Japan, the Philippines, and Sulawesi (Celebes). It is thought to be largely controlled in its major focus of infection, the Yangtze valley of China, where massive programs in the early 1950s were undertaken to control the snail and the parasite. It appears, however, to be increasing in the Philippines. Small foci of schistosomiasis have been discovered recently in Southeast Asia--Thailand, Cambodia, Laos, Malaysia, and Indonesia. The parasite in these foci appears not to be the same strain or form found in China, Japan, or the Philippines: additional evidence suggests that the distribution is more widespread than has heretofore been observed. Schistosomiasis is endemic in the Philippine islands of Luzon, Mindoro, Bohol, and Samar and is widely distributed in the islands of Leyte and Mindanao. In Sulawesi (Celebes), an endemic region has been known for some years in the area of Lake Lindu. In addition, there exists a zoophilic strain of S. japonicum in the island of Taiwan. The enzootic area is found on the West Coast in the Changhua district. Infection is limited to domestic and wild animals and apparently is not suitable for humans.

Estimates of the number of people infected with schistosomiasis throughout the world range from 100 to 250 million. The figure 180 to 200 million is a commonly quoted estimate. The disease has been found in 72 countries whose total population is 1,350,000,000. Nearly two-thirds of the 300 million persons living in Africa are thought to be infected. Estimates of the infection level in Egypt range from 30 to 75 percent, but it is commonly thought that more than half of the rural population is infected, a rate similar to that in Yemen where S. mansoni is particularly common. Perhaps 10 million of the 85 million population in Southwest Asia (Middle East) is exposed and approximately 3 million of those carry the infection of S. haematobium or of S. mansoni.

In the Orient, estimated infections varied from 30 to 90 million prior to the mass campaigns for the elimination of schistosomiasis from the Yangtse valley in China. How many still carry S. japonicum today is unknown, especially in China. The infection has not yet been eradicated though, undoubtedly, prevalence has declined dramatically. Similarly, infection in Japan has been markedly reduced and is now of minor importance; whereas in the Philippines, infections are increasing though exact data are not available. According to Warren (1971), of the 885 million dwelling in the Orient, 102 million are thought to be exposed and 33 million, infected. Estimates of prevalence in South America range from 8 to 10 million. In Brazil and Venezuela, infection is widespread and thought to be on the rise.

Estimates of prevalence throughout the world are based upon highly inaccurate census figures and largely unknown infection levels. Agricultural and water development projects in Africa have spread infection and increased prevalence to a marked degree. By contrast, in China and Japan and perhaps other regions, infections have fallen. The possibility of an accurate determination of worldwide prevalence of schistosomiasis is slight. However, it is reasonable to assume that between 100 million and 200 million people are infected; that a substantial number of those are diseased as well; that the disease distribution is changing and increasing in South America and in Africa; and that infections with these helminths represents one of the mose severe problems in terms of control, pathogenicity, and treatment of any of the parasitic diseases of mankind.

Epidemiology

Basic to any understanding of epidemiology, distribution, pathogenesis, or control of schistosomiasis is the need to understand the stages in the life cycle of the parasite and the conditions that control them. Many aspects of the schistosome species life cycles are remarkable, perhaps unique, among the digenetic trematodes. Among these are the presence of a fully formed ciliated larvae (the miracidium) within the eggshell when the egg is laid so it can hatch immediately upon striking water to release the rapidly swimming ciliated miracidium. Most fluke eggs hatch only after a variable period of development in the water and release their miracidia through a special eggshell lid, the operculum. Also, the presence of separate sexes is rare among flukes. Most trematode adult worms and monecious.

The adaptation of the free swimming cercaria larvae to water after its release from the snail and its instantaneous physiologic transformation after penetrating human skin to form serum-tolerant (and water-intolerant) schistosomules are also remarkable. The morphological and physiological adaptation of the adult worm to the human bloodstream is also extraordinary though obviously essential. The lack of a second intermediate host which enables the cercarial larvae on emerging from the snail to penetrate directly into the skin of the human host is of special epidemiologic importance.

From the egg through the snail phase starts with passage of eggs (via feces in the case of S. mansoni or S. japonicum; urine in S. haematobium) from an infected individual into the environment. The large, spined eggs when they succeed in reaching fresh water are stimulated to hatch instantly. They split longitudinally and each releases an actively swimming miracidium. With its short life of 4 to 6 hours, it swims ceaselessly, seeking a particular snail host in which it can develop. This search, if successful, is followed by penetration through the snail's epithelium directly into its tissues. The outer layer of ciliated cells is lost upon penetration of the snail and the emergent larvae is changed into a young, developing mother sporocyst. Although the miracidium may penetrate any of a number of snail species, or even nonmolluscan organisms, its development is restricted to the particular snail species to which it is adapted. Often only a particular strain or highly localized form can serve as the intermediate host in which the parasite can develop. In cases of penetration into an inappropriate or unsuitable host, the parasite is usually rapidly enveloped in host hemocytes and destroyed. Yet in the appropriate host, this sporocyst is not encapsulated and seems quite free of the host's blood cells.

The sporocyst coils up and develops a number of germinative bodies from cells within its elongated body. These progeny develop into a second generation of sporocysts, known as daughter sporocysts, which pass through the mother sporocyst wall and migrate into the liver or hepatopancreas of the snail to eventually occupy most of this large organ. Meanwhile, the mother sporocyst continues to grow and coil; it becomes an extremely large form in the tissues of the snail near the point of initial penetration. It continues to produce daughter sporocysts which migrate through the whorls of the snail into the liver and there enlarge into thick-walled, sausage-shaped forms. These in turn bud off a third generation of larvae known as cercariae--the characteristic fork-tailed larvae infectious to humans or other final hosts.

Some 4 to 8 weeks elapse in the course of development from the miracidium's penetration of the snail, through sporocyst generations, to production and release of cercariae which finally penetrate the human host. The period may be somewhat shorter for S. mansoni; under optimal conditions, only 4 weeks may be required. For S. japonicum, it ordinarily is 5 to 7 weeks.

From snail to final host phase starts when development of the fork-tailed cercariae is complete. These larvae leave the sporocyst in which they developed, pass through the tissues or circulation of the snail. and emerge into the water in swarms at periodic intervals. They swim rapidly with active thrashing of their forked tails and usually head toward the surface of the water. There they hang suspended by their tails, awaiting sensory cues, such as CO_2, which indicate presence of the final host.

In the case of S. haematobium, this is exclusively man with the possible exception of a few other African primates and a few rodent species. In the case of S. mansoni, humans again are the primary final host though wild infections are known in various rodents and primates. These probably are not reservoirs for human infection. S. japonicum, however, is able to infect a large number of mammals. This means that this species has a great number of reservoir hosts for human infection, such as domestic cattle, sheep, goats, and other herbivores as well as dogs, cats, and a wide variety of rodents. Almost any mammal exposed to S. japonicum cercariae may become infected.

Persons living in endemic areas generally cannot avoid contacting contaminated water. Most have rural occupations and depend upon frequent contact with water for irrigating, washing vehicles or animals as well as their children and themselves, laundering, performing ablutions, drinking, playing, and passing urine and excrement. Any contact, even as short as 3 to 5 minutes, may be sufficient for the cercariae to reach the surface of the skin and use the surface tension of the drying water droplet to assist its penetration. In the case of S. japonicum, penetration of the skin appears to require only seconds. Glands in the anterior end of the cercariae provide cytolytic or histiolytic materials that undoubtedly aid in penetration through the human skin. During penetration, the tail or swimming organ (for which the term cercaria is named) is discarded.

Development in the human host begins rapidly. In a matter of seconds, the cercariae is physiologically transformed into a dependent parasite called the schistosomule. It is able to migrate through the dermis into peripheral venules or lymphatics, after which it is carried passively through the bloodstream to the right side of the heart and into the pulmonary system. There, the young schistosomules remain for several days. It is not certain whether they manage to squeeze through the pulmonary capillaries, return to the heart, and become distributed via dorsal aorta and hepatic artery to the liver, or whether they pass out of the capillaries into the tissue spaces and then migrate direectly into the liver from the pulmonary area. By about the 15th day postpenetration, most of the surviving schistosomules are in the liver, where they grow rapidly while living on the nutritious foodbearing mesenteric blood.

The young adult worms migrate into the mesenteric veins and form semipermanent copulatory unions about 23 days postpenetration. The pairs consist of the hairlike, half-inch female and the somewhat shorter but much heavier-bodies males with tuberculated body coat and a copulatory ventral groove or gynecophoric canal in which the slender female is enclosed. It appears that male worms must be present in the liver to stimulate the females to mature. Once paired, the males with their stronger bodies and pair of anterior suckers migrate against the blood flow up the mesenteric system into their specific locality for final maturation and egg production. For S. japonicum, this is the superior mesenteric vein, its venules, and (for the females) the capillaries that enter the small intestine and surround the villi. S. mansoni is found in the inferior mesentery vessels around and within the wall of the large intentine; and S. haematobium, in the pelvic branches of the interior mesenteric venules.

Completion of the prepatent period and production of eggs occurs in about 5 to 6 weeks for S. japonicum, 7 to 8 weeks for S. mansoni, and approximately 10 to 12 weeks for S. haematobium. Egg production remains high and the female worms are able to produce for long periods, perhaps 20, 30, or even 40 years. The eggs of both S. japonicum and S. haematobium tend to be produced in clumps or clusters, which is of considerable importance in terms of the pathology induced. The eggs of S. mansoni more characteristically are produced and released singly. The eggs of all three remain alive and viable for about 20 days after they are laid in venules or capillaries. During this period, they must make their way through the human body, pass into fresh water in the outer environment, hatch, and release their miracidia. These, in turn, must locate and penetrate the appropriate snail intermediate host if the life cycle is to continue and produce another generation of schistosome worms.

Perhaps the most significant factor to be understood in the analysis of schistosomiasis distribution worldwide is the extremely focal distribution of the snail intermediate hosts that are responsible for transmission of the infection and for the ezquisitely delicate relationship between vector snail and parasite in adaptation of each for the other, so that individual strains or races of snail may be required for particular strains or races of the parasite for their survival.

Consequently, the mere presence of an identified intermediate host may not be sufficient evidence of compatability of that snail for the parasite in question without experimental confirmation.

Primary intermediate hosts of human schistosomes include members of the family Planorbidae in the case of S. haematobium and S. mansoni. The genera involved are Biomphalaria in the case of S. mansoni; and Bulinus in the case of S. haematobium. Several species within each genus are important as intermediate hosts of these two parasites. Their distribution patterns, presence and number of susceptible races, specific habits, biological characteristics, and preferences will determine the distribution pattern of subsequent human infection. In the case of S. mansoni, several species of the snail genus Biomphalaria are the key to understanding human disease distribution, e.g., B. glabrata and similar species in Brazil and elsewhere in South America and several islands of the West Indies, B. alexandrina in the Egyptian Nile delta region, B. pfeifferi and related species in Africa south of the Sahara, with still other species restricted to particular Great Lakes in the Rift Valley of East Africa. Similarily, particular strains or species within the genus Bulinus are the sole transmitters of S. haematobium. Many of these are members of the subgenus Physopsis, which are transmitters of human urinary schistosomiasis and some of the animal schistosomes as well. However, in addition to the subgenus Physopsis, the subgenus Bulinus, and in particular, Bulinus (Bu.) truncatus are important transmitters of S. haematobium and other animal schistosomes in Africa. Research in Ethiopia and elsewhere in East Africa has demonstrated that only specific genetic forms with multiple sets of chromosomes (polyploids) are capable of serving as intermediate hosts of S. haematobium.

In the Orient, a different family of snails is involved, the amphibious snail family Hydrobiidae. This family includes the genus Oncomelania of which five species appear to be the chief intermediate hosts. Their amphibious habit permits them to leave the water protected by their operculum which covers the shell opening and keeps them from dehydrating. Consequently, they often can escape molluscicidal treatment of the water--a prime factor in the epidemiology of the disease in that part of the world. Members of the genus Oncomelania responsible for transmission of S. japonicum to humans consist of O. hupensis in the Yangtse valley of China. O. nosophora occurs south of the important endemic region of the Yangtse valley and also on Honshu and Kyushu islands in Japan. This is the only host species in Japan. The third is O. formosana found in Taiwan. It is the only host of the animal-infecting or zoonotic form of S. japonicum found in Taiwan. The fourth, O. quadrasai, is the important intermediate host in the Philippines. Finally, O. lindoensis is the species found in Sulawesi (Celebes) in the Lake Lindu area in Indonesia. In addition, an extremely small hydrobiid snail, Lithoglyphopsis aperta, is thought to be the snail intermediate host for the isolated foci recently discovered in Southeast Asia (in Laos, Cambodia, Thailand, Malaysia, and Indonesia). L. aperta appears to be the intermediate host snail in Laos and Cambodia, but no intermediate host has yet been identified for the other more recently discovered foci.

Animal reservoirs are numerous. S. japonicum can infect a number of domestic and wild animal hosts. Cattle and dogs, in particular, are excellent reservoirs: the infection is able to sustain itself without any human infection to resupply eggs to the environment. Consequently, complete control of human infection will not prevent continuation of the life cycle. On the other hand, in Africa and the New World, S. mansoni is largely confined to the human host. Rodents, baboons, insectivores, and dogs may harbor the infection in certain areas of Africa, particularly in East Africa, but these are generally regarded as isolated instances of infection without primary feedback into the human life cycle. S. haematobium is still more anthropophilic since it is largely restricted to humans as the final host although rodents may play a minor part in the life cycle in parts of Central Africa. In general, however, neither S. haematobium nor S. mansoni could survive in nature without human infections to seed eggs into the freshwater environment in which appropriate snails are found: S. japonicum, on the other hand, is perfectly able to sustain itself without humans wherever it is found.

The role of human customs and behavior is important. This aspect of the epidemiology of schistosomiasis is too little appreciated in determining the exposure of individuals, particularly children. Human customs and habits are closely associated with the amount of seeding due to defecation or urination of infective eggs into water. In many Moslem areas of Africa, for example, the custom of disposing of human wastes in the river system is deeply ingrained. Cleanliness of the body is important, and the river is the sole means of such cleanliness. Ablution prior to prayer, as has been documented in Yemen, may unintentionally maintain the infection. Children playing in the ablution ponds will frequently defecate and urinate in them. Snails carrying the infection are present in these small puddles, and the religious members of the community who come to pray must wash their hands and face prior to entering the mosque. In doing so, they may well expose themselves to infective cercariae.

Similarily, habits of washing, of using public water sources as social gathering places, of bathing children, and of playing and swimming by children (the primary sources of egg seeding in nearly all cases) are all closely attuned to village, social, and racial customs and to belief patterns that are often influential in determining frequency, duration and manner of exposure.

Agricultural and other developmental projects have impacted on the spread of schistosomiasis. In recent years, massive hydroelectric programs in areas endemic for schistosomiasis have been completed: the damming of the Volta River in Ghana in West Africa, the Zambesi in Central Africa, and the Aswan High Dam to control the Nile. All three dams represent giant demonstrations of human engineering ability and possess enormous potential for industry, agriculture, and water control. Unfortunately, water in Africa means snails, and snails all too often mean schistosomiasis.

This indeed has proven to be the case with all three of these projects. Other smaller, hydroelectric developments in Africa and the Middle East have resulted in untold hardship and suffering due to the vast extension of schistosomiasis and the concomitant increase in intensity and frequency of infection in endemic areas. No solution to this problem is yet apparent. Its very complexity is a major deterrant to the control of schistotomiasis throughout much of the underdeveloped world.

Control Methods and Resources Available

No simple listing of factors that impinge upon schistosomiasis control can encompass the detail, complexity, and interactions among them. In general, as more details about schistosomiasis epidemiology are known, the greater is the chance a control program will attack the significant variables and succeed. Required information must include:

- specific parasite life cycle pattern;
- the biology of the intermediate snail host;
- the presence or absence of reservoirs (their number, distribution, and kinds);
- the habits of the human populations involved, particularly children as the prime sources of infection;
- the role of human societies, whether agricultural, hunter-gatherer, or urban-industrial;
- the special activities that may result in exposure or in contamination of water sources;
- the degree of development, movement of populations, changes and rate of change in peoples' habits in specific areas.

These variables are all involved in the changing pattern of schistosomiasis transmission so evident in recent decades.

In view of the extent and complexity of the problem, some epidemiologists and public health experts feel that control of schistosomiasis in areas of current development in Africa and South America is next to impossible. Others believe that with appropriate planning and supervision of new development projects, there is a real possibility of modifying conditions to keep schistosomiasis from rampant spread.

Possible control methods are available. The major responsibility of any committee or group given the responsibility for planning schistosomiasis control is to determine which of several different strategies should be employed. These include:

- chemical or biological snail control;
- treatment of affected individuals;
- mass treatment of the exposed population;
- modification of the community way of life to avoid contamination of water sources;

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- modification of the environment to reduce exposure and contamination, and
- change of snail habitats to restrict their ease of multiplication and survival.

Several strategies should be combined in most situations. All have been tried with varying degrees of success. A decision made early in the planning phase on the objectives and approach to follow obviously is crucial to the success of the resultant program. One large-scale experiment has been organized to test several strategies under relatively similar conditions. This is the program in St. Lucia, sponsored by the Rockefeller Foundation, underway since January of 1972. Three valleys on the island were selected. In each, a different approach to the control of schistosomiasis was followed.

In one, the emphasis was on reduction of water contamination with S. mansoni eggs by treatment of the infected individuals. In the second valley, reduction of cercarial density was attempted chiefly by chemical snail control. In the third, reduction of water contact was established by providing a safe water supply and restricting access to infected water sources. A fourth area was left untreated as a control. In each area, precontrol assessment was carried out to secure baseline data and to develop techniques for application and evaluation of the results. Recent publications, to the surprise of many observers, indicate that chemotherapy proved to be the least expensive and the most efficacious of the three approaches attempted (Jordan, 1978). However, wide application of this result in other areas may not be possible. Yet the findings are significant and represent the first careful attempt to evaluate different strategies for schistosomiasis control.

Snail control has been the most commonly followed control measure, primarily because it can be done in a mechanical fashion by a team entirely independent of affected villagers. Molluscicidal chemicals are applied at regular intervals, often in conjunction with snail habitat modification by clearing of vegetation from infected water ways, especially irrigation ditches which are readily cleaned. The molluscicide may be applied in various forms; pellets, powder, in a slow-release rubber matrix, or in a vehicle to keep it at a given depth to avoid burial in mud. Niclosamide and Bayluscide, molluscicides generally employed today, are extremely toxic to fish and may pose other biological hazards to microorganisms or elements of the food chain. These chemicals are lethal for snails even when diluted to fractions of one part per million. Nonetheless, the continual application of such highly toxic compounds to public water supplies is hardly an optimal approach to the problem of snail control.

Furthermore, the independence of control teams from the villagers and high cost of these imported molluscicides makes it a certainty that this approach to snail control will require continued external support. When mollusciciding is over, the snail population will, without any other control measures, rebound to its former level. If sources of eggs are not restricted, snails will soon be reinfected and shedding cercariae; and conditions will revert to those in existance prior to the beginning of the control program. This method, therefore, must be a permanent one if snail control is to be a primary means of reducing or controlling schistosomiasis in an area.

Another approach to snail control popular with both scientific and lay public but extremely difficult to develop and apply is biological control of snails. A large number of snail predators, competitors, parasites, and pathogens have been described, studied, and tested in the laboratory and occasionally under field conditions. Generally, they do their job relatively well and under isolated or controlled conditions appear to eliminate or modify snail populations. However, these applications generally are made under very restricted conditions and, when extended, prove to be subject to other biologic forces and often cancel their effectiveness or render them counter-productive.

One approach has been the use of snail Marisa, which competes for host snail space and food and devours eggs of the target host snails. It appears to have been useful in certain areas of Puerto Rico where it was tested, but applications elsewhere have failed or been withheld because of the possibility that Marisa might consume agriculturally important crops, serve as an intermediate host for other trematode parasites, or simply fail to reduce target snail numbers under widely varied ecological conditions. Similar problems are likely to appear with other biological controls, given the impossibility of predicting new biological interactions once the control agent has been released into the environment. A review of this approach, written by Fergusen, will be found in Miller (1972).

Chemotherapy as a control measure raises the problem of toxicity of the trivalent antimony compounds and other drugs that have been employed. Though less toxic, these other drugs are not suitable for wide use either because of the multiple applications required, the need for injection in most, the high cost in all but one, and the possibility of long-term effects (teratogenicity, mutagenicity, carcinogenicity). But more important as a deterrant to use of these drugs is the uncertain cure rate which varies with patient age, duration of infection, and the species of parasite present. Since dosage depends on body weight and many constraindications to use of these drugs exist, the danger of mass chemotherapy is obvious. Nonetheless, over 300,000 doses of the single-injection drug, hycanthone, have been given in Africa and South America.

Studies at Johns Hopkins University by Bueding and associates suggest that hycanthone should be withheld from use because of mutagenicity and cancer production in experimental rodents. Hycanthone was the drug used on St. Lucia where it was considered the most successful of the strategies tested. Until general agreement is reached about the feasibility of a particular drug, there is little likelihood that chemotherapy will be used on a wide scale, although this remains an obvious and promising approach.

Construction of sanitary toilet facilities or design of safe and culturally compatible methods for disposal of feces and urine is a primary--and often surprisingly difficult--strategy for schistosomiasis control. Unless the facility is acceptable, it will be ignored. Often our assumptions as to "normal" privy construction or disposal methods are entirely foreign and inappropriate to the people concerned. Design of toilet, bathing and laundry facilities too frequently break cultural codes and disregard local sensibilities. The new facilities remain costly and worthless enterprises which are quickly abandoned or disregarded, while the people continue to drink, bathe, launder, urinate, and defecate directly in the water as they may have done for ages past. A sympathetic, sensitive, and understanding educational program is required if the fundamental problem of safe disposal of human wastes is to be satisfactorily solved.

Safe delivery of water supply into houses or uncontaminated village centers is perhaps the most important protective health measure that can be instituted. During construction of the Aswan dam and other major hydroelectric power programs in Africa, hundreds of thousands of people were relocated into newly built villages or compounds. Frequently, this resulted in increased schistosomiasis. Yet it was found in investigations in Upper Egypt by a University of Michigan team working collaboratively with the Egyptian Ministry of Health that villages relocated a half mile or more from irrigation ditches and supplied with piped water had a dramatically lower schistosome level than did villages moved closer to these infected waters.

Families or villages settling alongside irrigation and other water sources swiftly contaminated them. Snails were often there as soon as the people were--and schistosomiasis levels surged to eighty or ninety percent of their former levels in less than a year. In villages farther from the source of infection, children were not conveniently located near the streams and could not swim and play for extended periods in infected water. Infection rates here were approximately thirty percent of former levels. Still, these rates are considerably higher than the ones found in the desert dwellers that first lived there (about 5%): yet they are significantly less than levels reached in villages located alongside infected waterways.

Engineering approaches have been employed to alter the irrigation ditches by lining them with concrete; to remove vegetation and snails by increasing the rate of water flow through the canals; to change the water level rapidly; to introduce weirs and other forms of screening or obstacles to snail movement. Each of these methods is obviously limited by cost and maintenance problems. In some parts of South Africa and in East Africa, teams clear vegetation continuously from irrigation ditches (and, surprisingly, have no higher levels of infection than the rest of the population). These methods must be applied in high density or high production areas where economic feasibility justifies the cost and the continuous maintenance required. In general, such approaches for modification of snail habitats are useful adjuncts to other control methods, but not sufficient in themselves.

It needs to be pointed out that other economic assistance projects funded by international or national organizations tend to enlarge vastly the breeding space for snails, increase probability of exposure and extent of human infection, and serve to extend the range of the disease rather than control it. These increases are due to agricultural development, irrigation ditching, hydroelectric programs, and vast extensions or stabilization of the water distribution system. Consequently, no permanent disease control or even modification of the current pattern of extension is possible unless both schistosomiasis control efforts and agricultural expansion efforts are planned, funded, and implemented jointly.

Restriction of access to contaminated water has been tried. Fencing and other means to keep children from restricted areas of high snail density, pollution, or snail population infection levels have been a-tempted in St. Lucia and a few other localities where transmission was presumed to be high. These restrictive efforts sometimes succeeded, but more often failed. Fences are invitations for children to dig under, climb over, or otherwise evade. Again, engineering attempts are successful only to the degree that they are accepted by the resident population. The key is understanding and sensitivity to the needs and feelings of the resident people and an attempt to work with them through their own leaders for selection, modification, and acceptance of an appropriate method for infection control.

Immunization is essentially a hope for the future--but it will be a simple and probably socially acceptable method if it works. At the present time, one can only encourage the research needed for success. An optimistic estimate of the time needed to test this strategy is about ten years.

It is evident that no single strategy is sufficient. Yet to attempt all of them together would make a burdensome, unwieldly, and excessively costly undertaking. Therefore, it is incumbent upon those responsible for the control of schistosomiasis to select those control methods best adapted to the specific region and the needs of the people involved.

Schistosomiasis is an inordinately complex disease, but fortunately it has one of the best indexed and most complete set of bibliographic materials available in any biomedical literature. The most important compilations of references and specific references on control are included at the end of this paper. (See citations under Warren, Ansari, and Miller).

Data on the incidence and prevalence of schistosomiasis are not readily available and what can be found is surprisingly incomplete, inconsistant, and unreliable. The principal sources of information are major universities, governmental institutions, private foundations, international organizations, and health departments in endemic areas. Probably though, information most vital for control programs will be produced by current schistosomiasis control and demonstration projects. There are 26 such projects in progress: 6 in the Americas; 7 in the Middle East; 11 in Africa, and 2 in Asia. The responsible agency for these projects is predominantly the government of the country concerned. One project is privately financed and one supported by WHO. A list of these projects can be found in Miller (1972).

Few of the current schistosomiasis research programs are primarily devoted to control methods. One exception is the Rockefeller Foundation program on St. Lucia, an island in the Caribbean, on which series of studies have been performed over the last few years to test various control modalities. In general, however, experimental research tends to be the work of individual investigators who focus on specific problems. Applicable research undertaken in the U.S., Great Britain, and elsewhere is mainly directed to development of tools that could be employed for improved control efforts.

Chief among these is a long-continuing effort to develop a vaccine, a mass preventive or mass therapeutic approach. At present, it seems no such panacea is likely to be available for many years. However, skin tests that utilize a highly purified antigen to eliminate nonspecific reactions are under development. If the dermal response demonstrates sensitivity as well as selectivity in field trials, such tests could be of great value in broad surveys to estimate past exposure or, perhaps, current infection. The latter is less probable if this new test is similar to skin tests now available. Research on other techniques is devoted to improvement of methodologies for quantitation of egg counts, including electronic readout of egg samples in fecal or urine specimens.

The majority of schistosomiasis research programs are directed toward an improved understanding of the immune process and host response to schistosome antigens in the human body. A wide range of reactions have been described: some elicited directly by the parasite and others, as a secondary host response which may be pathologically directed. Development of chemotherapeutic drugs has been restricted because of problems associated with governmental requirements, the high cost of drug research, inhibitions in testing drugs on human populations, and limited resources in endemic areas for the purchase of these costly compounds. The United States Walter Reed Army Institute of Research has continued to sponsor schistosomiasis and malaria drug therapy studies. Several promising new drugs are being tested; these are not yet ready for wide therapeutic application, particularly for the massive use required in a widescale schistosomiasis control program.

Organization and Phases of Control

The organization of existing control programs is as varied as the landscapes in which they are found. A summary of the organizational modalities in an effort to formulate a single set plan would be simplistic and of little use. The extensive manual on epidemiology and control of schistosomiasis prepared through WHO by Dr. Nasser Ansari (1973) does review these approaches and provides extensive practical information on survey forms and procedures. There is little advantage in restating the details given there. Consequently, the work of Ansari and of the eminent contributors to that volume should be considered the basic manual for organization, surveillance, and evaluation of any schistosomiasis control program.

More restricted in scope and size is the volume edited by M.J. Miller (1972) on the future of schistosomiasis control. These two works represent a state of the art message on the feasibility and organizational information required for schistosomiasis control programs. In view of the extraordinary diversity of these programs, their varied goals and the procedures followed, it is impractical and inappropriate to consolidate their procedural guidelines into a single format. One difficulty faced in attempts to simplify and systematize program organizations for schistosomiasis control is the variety of objectives proposed, even in the same general region, to achieve the same end--the reduction or control of schistosomiasis.

An example is Farooq's statement in the Ansari (1972) manual: "It is interesting to note that in dealing with the same species of parasite, different countries have emphasised different approaches. These include ecological control of snail habitats through water management and improved land use and agricultural practice; mass therapy; chemical, physical, and biological controls of snails; environmental sanitation; or a combination of two or more of these, with varying degrees of emphasis placed on the different aspects."

Each of these requires not only different organizations but different staff, training procedures, levels of funding, and degrees of population involvement as well as different objectives and criteria for measuring success. WHO has played a key role in preventing duplication of experimental efforts and in offering increased opportunity, through publications and meetings, to consider the relative merits of different approaches in various countries.

Any control scheme adopted must be carefully organized and based on accurate information about the needs and conditions of the specific control target--whether disease agent, snail hosts, environmental controls, or infected human population. This may require data on: distribution, infection rates and seasonal periodicity of snail hosts, bionomic studies of the snail fauna in a particular area, or cost analysis of the economic impact of disease. The following will probably be needed also: information on disease endemicity and severity based on accurate mapping and precise location of human infections; location of probable transmission sites; evaluation of human habits, occupations, and water contacts with respect to irrigation and farming practice, recreational activities, and domestic and religious habits.

It is necessary to gather this information before a preliminary plan can be established; field teams organized and trained; equipment, schedules, supervision, and funding clarified; and the protocol finalized. Given sufficient data, the will to undertake the program, and sufficient financing, methods for control of schistosomiasis do exist. Yet despite the feasibility of control, only China has achieved long-term success in eliminating the disease from large areas. Control programs usually have been designed as pilot projects or demonstration programs. Those maintained for longer periods ultimately became diluted with other public health activities and lost much of their focus and effectiveness. Widespread interest and concern about schistosomiasis exists and considerable funds are available, but project after project has failed to provide the sustained thrust and motivation necessary to make a lasting impact on disease transmission.

There are a few general characteristics that are necessary for any control program to operate effectively. For example, the basic scheme must utilize a team approach to design the overall strategy and develop the protocol. This must involve continuing collaboration of epidemiologist, public health administrator, sociologist, engineer, biologist, clinician, and the leadership

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of local residents. The skills of each are essential, but most important is the integration of these skills into a single mold. The proper mix of medical, biological, and behavioral sciences will sustain the broad base required for understanding the complex disease problems that are involved in this disease, which is an outstanding example of interaction among disease agents, reservoir and intermediate hosts, and the human patterns of life fundamental to the transmission process. The sociocultural aspects must be considered primary factors to be understood in order to eventually control schistosomiasis.

Staffing control programs must be utilized. Adequate staff with experience, reliability, and dedication is essential for the success of any control program. Equally important is the separation between the afflicted populace and the team responsible for temporary control of their problem. Those who are recruited, trained, organized into teams, and sent into the field to take part in the day-by-day operations tend to be isolated from local residents and sometimes even in conflict with them. Rapport is seldom established so that when the job is done and the experts or trained personnel leave, the situation gradually deteriorates to its former condition. Snails quickly repopulate an irrigation canal and within weeks or months of the cessation of molluscididing operations, the snail population and infection rate approaches precontrol levels.

Maintenance of sanitary or water control facilities is equally essential to prevent reinfection in humans which otherwise is bound to recur--and may well do so in any case. Short term contractual tasks by a team of elitist workers or supervisors has little bearing on the long-term welfare of the people. The problem is one of recruitment and training plus integration. The difficulties of these tasks are evident and are clearly illustrated by the lack of success in using control programs as a means to establish a mechanism through which local occupants can assume responsibilities when control personnel leave.

The availability of staff, adequacy of training, and suitability of current control efforts cannot be reviewed in general terms. Funding, recruitment, and administration of each project is so distinct that no two staffing projects have had the same problems or results. This discussion is simply to emphasize that staffing problems are essentially those of finding, recruiting, training, stimulating, and sustaining expert control teams while maintaining strong liaison with the local worker staff. Hopefully, recruitment within the village populace can be effected to ensure continuity of control by maintaining certain aspects of the control program after external staff leave. In addition, it is particularly difficult to hire specialists who will see the program through, especially staff from academic institutions. Most of these individuals can spend only one or two years in the field, and their dedication to the program is constrained by other professional and personal commitments. Part of the program plan should be to incorporate villagers as well as professionals into project staff. Additionally, a communications channel with local chiefs, leaders, or elected officials as well as individuals who work with the project should be maintained.

A careful outline of the procedures to be followed in the organization of a control program has been prepared by Farooq in the Ansari volume (1973). He emphasizes the need for a National Committee for Schistosomiasis in each endemic country. The Committee should be composed of representatives from all of the agencies involved and meet on a regular schedule to insure desired and essential cooperation on a continuing basis. Farooq divides the stages into preparation, operation, surveillance, and conclusion of the program.

The preparatory phase required preliminary data that establish the endemicity of the disease and estimate prevalence of human infection. Preliminary data should also provide a distribution of cases by age, occupation, geographic location, and severity of infection. Provision must also be made for continuing surveys of intermediate hosts and infection surveillance. Proof of the role of suspected snails requires more than identification: it must include examination of wild snails for naturally acquired infection in laboratory animals with field-collected cercariae and demonstrate infection of healthy snails with miracidia from eggs passed by test ordents. Positive, specific identification of the snail host must also be made. This often requires the service of a skilled malacologist who may not be available in the local area. For this purpose, WHO maintains a snail identification center at the Danish Bilharziasis Laboratory in Copenhagen and at the Institute of Biology, University of Brazil.

When these steps are completed, the snail distribution area must be accurately mapped: observations of their bionomics must be made also and those related to patterns of nearby human activity. A search should be made for possible animal reservoirs or the presence of animal schistosomes that may infect man. In some areas of Central Africa, this may be quite a complex undertaking as a number of herbivore species of schistosomes are present. Some of these (e.g., Schistosoma intercalatum) are known to become human parasites.

With this necessary advance information, with organization of the team to ensure collaboration of the various specialists needed, with establishment of a National Committee to organize, control, monitor, and evaluate program results, the preparatory phase can begin. The three elements of the preparatory phase are initial survey, pilot operation, and verification of the efficacy of the methods and organization proposed.

After the initial surveys have been completed, schedules can be prepared and estimates made of activities to be carried out during the subsequent attack phase. These steps should be completed prior to recruitment, personnel training, and establishing the administrative structure. Success of the program depends, to a significant degree, on the care and thoroughness of these preparatory stages. The dynamics of the control program itself can then be based upon actual knowledge of specific areas rather than a textbook organizational format.

The attack (or operational) phase is then organized based upon the findings and recommendations of the preliminary plan. The organization, scope, cost, and final plan will depend entirely on the methods and objectives best suited to the conditions and region. These may be snail destruction by molluscicidal treatment; engineering efforts for water and sanitary control; or clinical evaluation and treatment of selected members of the infected population. Although planning, organization, and supervision of the control scheme will vary greatly, depending upon the strategy selected, there are general characteristics common to all of them. For example, there must be a clearly defined, measurable objective. The timing and nature of the plan must be clearly spelled out--what it can accomplish, how long it will take, how much it will cost, and what steps are to be followed in sequence to carry it out. This must be clear not only to the planner but to all levels of leadership and to the workers in the field. The plan should be simple. With ambiguity, there is danger that it will become deeply involved in misdirection and misunderstanding. The simpler the organization and the plan itself, the greater chance it has of success.

There must be a means of proper analysis and classification of the procedures used. The actions to be followed must include establishment of standards and means to monitor them. The plan must be flexible, capable of adaptation to meet situations that are bound to change. It should use available resources to the utmost. It goes without saying that resources are limited, particularly in the tropical areas where schistosomiasis is most prevalent. Consequently, effective use must be made of all available personnel, resources, expertise, and facilities.

Farooq, in his discussion of the organization of schistosomiasis control scheme, goes on to describe the organizational elements that follow once the plan has been agreed upon. He encourages use of modern management techniques to ensure that the working force is of sufficient quality, that initiative is encouraged, and morale of the working group is maintained. This, he feels, is more important than rigid discipline. Training must be based on careful selection and sustained throughout the project as a conscious and continuing process. Proficiency is not based on skill alone but must utilize available energy and latent ability. Potential qualities can be drawn out by proper guidance, direction, and stimulus from the administrators.

This may well prove to be the key element in any plan and organization for schistosomiasis control. Most programs have been essentially thrust upon the local population; their participation is required only as laborers or as tolerated witnesses. Little effort is made to assure their understanding of its purpose or design. On the other hand, if a project can be tied culturally and socially to local activities, the people most affected are stimulated to join the group rather than observe it from the outside. There might then be reasonable hope that long term continuation of schistosomiasis control in such an area could become a reality.

Evaluation and monitoring of control programs are essential for success and continuation. Comparisons must be made of conditions before, during, and after completion of the project if the results are to be meaningful. Farooq clearly stated the issue and importance of this phase of the program (1973): "Evaluation should start at the inception of the program and be recognized as an integral and continuous part of the responsibility for running it. Evaluation procedures have, therefore, to be built into the plan and should constitute its essential ingredient to be pursued continuously. In evaluation, such elements as reliability, validity, performance, cost, and public acceptance should be studied. This requires meticulous skill and scientific methodology to obtain unbiased results."

Details of the evaluation and control programs are considered by L.J. Olivier in another chapter of the 1973 Ansari manual. Among the topic headings that are considered important by Olivier in his evaluation and discussion are the following (Ansari, 1973):

(1) Measurement of efficacy in terms of human infection and disease
  (a) evaluation by study of the total prevalence of infection
  (b) evaluation by study of prevalence in children
  (c) evaluation by study of change in intensity of infection
  (d) evaluation by study of the clinical gradient
  (e) evaluation by objective study of damage to infected persons.
(2) Evaluation of efficacy using indirect evidence
  (a) evaluation by study of snail populations
  (b) evaluation by study of infections in snails.
(3) Other possible supplementary methods for evaluation.

Of great importance in monitoring and development of evaluation procedures for these control programs are the record keeping, survey, and other forms to be employed. Techniques for census and population surveys require sophistication and expertise; but still, the questions asked must be in keeping with the educational levels of the populations surveyed. These are considered in some detail in the Ansari manual and must be evaluated specifically for each particular type of program.

Determination of Cost Effectiveness

Cost effectiveness runs into the still unsolved problem of determination of the impact of disease. Attempts have been made to ascertain effects of schistosomiasis on economic productivity of the population, on social well-being, on learning ability in school, on work capacity, or on any measurable criteria that could be employed to measure specific effects of schistosome worms in the human body. Inasmuch as most infections are light, the disease long-lived, conditions of extreme pathology generally rare and late in appearing, there is no simple way by which one can measure either the impact of the disease or the benefit of release from infection. For the majority of people, it may well be that modification of conditions so that they no longer retain their small number of worms would hardly be noticed. However, the effort required to care for those who are indeed sick and the gradual accumulation of eggs and the human response to them among millions of the 200 million infected individuals causes immeasurable but, nonetheless, great human suffering. Their relief, undoubtedly, is worth the cost of any control program however difficult that cost may be to ascertain.

A brief review of the economic implications of schistosomiasis is given by J.G. Cummins in Miller (1972). In this discussion, Cummins attempts to marshall evidence for reduction of work capacity and other economically measurable effects of schistosomiasis on the population. He concludes with the feeling that it is quite clear that underdeveloped nations remain penalized to an extraordinary degree by schistosomiasis and other tropical infections. However, in spite of the large amount of research on this disease, there are very few data suitable for economic benefit or cost analysis evaluation. Additional research which could develop methods adaptable for studying the effect of schistosomiasis on working populations would be extremely useful. Burton Weisbrod (1973) of the University of Wisconsin has made an extensive study of the economic impact on work behavior, learning capacity, and other human functions in St. Lucia. His results indicated great difficulty in distinguishing between infected and noninfected individuals--which helped to point up the problem if not the solution.

Conclusions

The one lesson repeatedly learned in the course of 50 years of efforts to control schistosomiasis in tropical regions is that there is no such thing as an ideal surveillance and control program. Each aspect of the disease--which includes human and other hosts, snail intermediate hosts, the pathological agent itself, and the circumstances under which they interact in specific communities or regions--all introduce variables that cannot be constrained within a common, idealized format. Priorities depend, for example, on the strategies selected; the timetable depends on the local conditions in which the resulting program is to be developed. Resources required are restricted by funding, personnel selected, local conditions, and nature of the specific plan developed.

A sober thought on schistosomiasis control entrenched in the minds of all specialists working in this field is the unqualifiedly poor record achieved so far. With each movement of water into new regions in endemic areas, movement of host snails has exceeded the capacity of the control projects to contain them. Concomitantly, migrations of infected peoples into these new areas, rapid infection of snails, and establishment of new transmission foci have been markedly successful, whereas control of these processes have been markedly unsuccessful.

Success has been limited to confined areas where the problem is simpler, funds more available, and economic justification sufficiently great to encourage very strong governmental activity to focus on a particular problem area or region. This has been true in sugar cane plantations in Tanzania, to some degree in the Gezira project of the Sudan, in Puerto Rico, St. Lucia, in the Faiyum of Egypt, in Rhodesia and South Africa, and a few other isolated areas. With the exception of these specific successes, the rate of achievement is a dismal record, one that serves as a continuing warning to future planners to consider each local situation in terms of the needs of its people and the ability of the controlling agency or program to work within their requirements. This type of integrated effort hopefully would lead to an ongoing local campaign, as in the Chinese example. It is, of course, naive to assume that a mass program such as that of the hundreds of thousands of enthusiastic Chinese workers and farmers could--or should--be elicited in Africa or South America to generate the effort required. However, the message seems clear that integration of effort and some degree of joint activity with the population concerned are necessary for long-term success in any such effort.

Schistosomiasis remains the major helminthic disease problem of the world's tropical and subtropical regions, particularly in Africa and South America. It is continuing to spread in both of these regions in spite of extensive efforts to contain that spread. Epidemiologically complex and varied, it remains largely intractable to control without massive, continuous efforts. Extensive new control programs are being planned by WHO, AID, World Bank, and other agencies. The degree of success reached will determine the chance for 200,000,000 people to come closer to their genetic capacity. As with the successful completion of the Panama Canal in 1903 which followed previous failures caused by malaria, yellow fever, and dysenteries, successful emergence of hundreds of millions from physical and economic bondage to disease and poverty may well depend upon success in the forthcoming campaigns against human schistosomiasis.

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